Acta Genetica et Statistica Medica

Vol. II | 1951 | Fasc. 3

INDEX

BASEL (Switzerland) S. KARGER NEW YORK

Printed in Switzerland

The „*Acta Genetica et Statistica Medica*" is issued quarterly. Each issue has approximately 96 pages. The annual subscription rate is Swiss frs. 44.—.

No payment is made for contributions, but 50 reprints of the article will be sent to the author free of charge. Extracopies, if desired, will be supplied at a special rate. The cost of the engravings will be borne by the publishers, provided the figures and graphs are suitable for reproduction and do not exceed a reasonable number. Otherwise the author after due notification, will be charged with the additional cost. Articles will be printed in English, French, and German, with summaries of about 10 lines. As a rule only original papers can be accepted.

All manuscripts should be addressed to *Gunnar Dahlberg*, State Institute of Human Genetics and Race Biology, Uppsala (Sweden). Corrected proofs, review copies, however, as well as enquiries concerning subscriptions and notices, should be sent to the publishers, *S. Karger Ltd.*, Holbeinstrasse 22, Basle (Switzerland).

Les „*Acta Genetica et Statistica Medica*" paraissent en fascicules trimestriels d'environ 96 pages. Le prix de l'abonnement annuel est de frs. suisses 44.—.

Les collaborateurs reçoivent à titre d'honoraires pour leurs travaux originaux 50 tirages à part gratuits. Les tirages à part supplémentaires seront facturés à un prix modéré. La maison d'Edition se charge des frais de clichés à condition qu'elle reçoive des originaux se prêtant à la reproduction et dont le nombre ne dépasse pas la mesure strictement nécessaire. Autrement les frais supplémentaires seront, après avertissement, à la charge de l'auteur. Les travaux pourront être rédigés en langue anglaise, française ou allemande et doivent être suivis d'un court résumé d'environ 10 lignes. Ne seront acceptés en principe que des travaux originaux inédits.

Tous les manuscrits sont à adresser au Prof. Dr. *Gunnar Dahlberg*, State Institute of Human Genetics and Race Biology, Uppsala (Suède). Les épreuves corrigées, les ouvrages à analyser, de même que toute correspondance concernant les abonnements et la publicité sont à adresser à *S. Karger S. A.*, Editeurs, Holbeinstrasse 22, Bâle (Suisse).

Die „*Acta Genetica et Statistica Medica*" erscheinen vierteljährlich in Heften von etwa 96 Seiten zum Jahresabonnementspreis von Schweiz.-Fr. 44.—.

Mitarbeiter erhalten für ihre Originalarbeiten an Stelle eines Honorars 50 Sonderdrucke kostenfrei; weitere Separata gegen mäßige Berechnung. Die Kosten der Clichés übernimmt der Verlag, soweit reproduktionsfähige Vorlagen geliefert werden und die Zahl der Abbildungen das notwendige Maß nicht überschreitet. Andernfalls gehen die Mehrkosten zu Lasten des Autors und werden vorher mitgeteilt. Die Arbeiten können in englischer, französischer oder deutscher Sprache eingereicht werden und sind mit einer kurzen, etwa zehnzeiligen Zusammenfassung zu versehen. Es werden grundsätzlich nur unveröffentlichte Originalarbeiten angenommen.

Alle Manuskripte sind zu richten an Prof. Dr. *Gunnar Dahlberg*, State Institute of Human Genetics and Race Biology, Uppsala (Schweden). Korrigierte Fahnen, Rezensionsexemplare sowie Zuschriften, Abonnemente und Inserate betreffend, sind an den Verlag *S. Karger A. G.*, Holbeinstraße 22, Basel (Schweiz) zu senden.

Travail de la Clinique Ophtalmologique de l'Université de Genève.
Directeur: Prof. A. Franceschetti

LE LINKAGE AUTOSOMIQUE CHEZ L'HOMME

et sa recherche par la méthode de Penrose [1])

par W. TAILLARD

Introduction.

Lorsque deux gènes conditionnant deux caractères différents sont localisés sur un même chromosome, on dit qu'ils sont liés, ou associés, et l'on parle d',,association entre facteurs", de ,,linkage" ou de ,,Koppelung".

L'étude du linkage a fait l'objet de nombreux travaux expérimentaux et a largement contribué à l'établissement de la théorie actuelle du mécanisme de l'hérédité. Point n'est besoin de citer les brillantes recherches de *Morgan*, *Bridges* et de leurs collaborateurs sur la drosophile, recherches qui établirent pour la première fois l'existence du linkage. Les travaux de toute une pléiade d'auteurs ont mis en évidence des associations entre facteurs chez les végétaux inférieurs et supérieurs, chez les invertébrés et les vertébrés (rat, lapin, souris) et ont établi la réalité et l'universalité du phénomène.

C'est également par l'étude approfondie du linkage et du crossing-over que l'on a pu établir les cartes chromosomiques, c'est-à-dire, la localisation précise des gènes sur le chromosome, et leur position respective les uns par rapport aux autres (carte chromosomique de la Drosophile surtout). On a également pu montrer qu'il existait autant de groupes de gènes liés entre eux que de paires de chromosomes; ainsi, chez la Drosophile, qui possède 4 paires de chromosomes on put répartir en 4 groupes les 300 caractères héréditaires connus. On put aussi distinguer 2 sortes de linkage: Le sex-linkage, où les gènes liés sont localisés sur le chromosome sexuel ou hétérochromosome, et le linkage autosomique, où les gènes liés se trouvent sur les autres chromosomes, ou autosomes.

---

[1]) Travail fait dans le Service de Génétique de la Clinique sous la direction du Dr. *Klein*. Communiqué lors du Congrès d'Anthropologie Différentielle (Paris, 11–16. IX. 1950).

Lorsque l'on voulut appliquer à l'échelle de l'homme les résultats des travaux expérimentaux, on se heurta aux nombreuses difficultés rencontrées dans tous les domaines de l'hérédité humaine : petit nombre des descendants, grand nombre des chromosomes, impossibilité de faire des mariages à la guise du chercheur, lenteur avec laquelle se suivent les générations etc.... (*Guyénot*). C'est pour celà que la génétique humaine a dû faire appel aux méthodes statistiques, de façon à pouvoir grouper les faits, et à les interpréter correctement. Celà explique aussi la lenteur avec laquelle progressent ces recherches et la nécessité de recueillir un grand nombre d'observations avant d'oser émettre une hypothèse et à fortiori de la certifier.

Le linkage chez l'homme a cependant fait l'objet de nombreux travaux traitant pour la plupart du sex-linkage, travaux de statisticiens, de médecins, de pathologistes etc.... (hémophilie, Daltonisme sont parmi les caractères les mieux étudiés). Toutefois, l'étude du linkage autosomique a fait tout de même, durant ces 20 dernières années de grands progrès:

C'est en 1926 que *L. H. Snyder* publiait sa première étude sur le linkage autosomique; il décrivait une méthode pour le mettre en évidence, et il essayait en vain d'établir une connection entre les yeux bleus et les groupes sanguins. L'année précédente, *Straszynski* avait tenté de relier les groupes sanguins et la rapidité avec laquelle certains syphilitiques négativaient leur W. A. au cours du traitement.

En 1931, *Bernstein* mettait au point une méthode statistique pour la détection du linkage, et était suivi par *Hogben* (1934), *Fisher* (1935), *Haldane* (1934), *Finney* (1940–1941) et *Haldane* (1946). Les méthodes de tous ces auteurs présentaient l'inconvénient d'exiger, soit la connaissance exacte du mode de transmission héréditaire des caractères considérés, soit l'examen des parents et quelquefois des grand-parents des familles étudiées, ce qui trop souvent compliquait les recherches ou les rendait impossibles. Aussi, toutes ces recherches ont elles abouti pour la plupart à des résultats négatifs; cependant, elles ont tout de même permis de découvrir quelques linkages:

Wiener (1932) utilisant une méthode voisine de celle de *Bernstein*, montrait que les groupes sanguins se transmettent indépendamment des types sanguins (M et N), *Hogben* et *Pollack* (1935) trouvaient une indépendance entre le P.T.C. et les groupes sanguins, ainsi qu'entre la brachydactylie et la maladie de *Friedreich*. *Zieve*, *Wiener* et *Fries* (1936) examinaient 66 familles sans trouver de linkage entre les types sanguins, l'allergie, et la couleur des yeux

(Méthode de *Finney*). *Finney* (1941) ne trouve aucune liaison entre les groupes et les types sanguins, le P.T.C. et le sexe. Par contre il applique sa méthode aux résultats de *Zieve*, *Wiener* et *Fries* et met en évidence un linkage entre les maladies allergiques et les groupes sanguins. Ce linkage n'est cependant pas confirmé par *Haldane* (1946). Enfin *Snyder* (1947–1949) vient de publier une nouvelle association établie par la méthode de *Finney*, entre les types sanguins MN et N et l'anémie à cellules falciformes.

L'étude du linkage autosomique a fait un très grand progrès depuis que *Penrose*, en 1935, publia sa méthode dite du 2 × 2 ou „sib-pair method", méthode qu'il perfectionna en 1938 par la „graded character method" et en 1946 par la méthode dite du 3 × 3. Le principe de ces méthodes, comme l'a exposé récemment *Franceschetti* (1949) repose sur la comparaison des frères et sœurs (sibpairs) d'une même famille (sibship).

Dans les mains de plusieurs auteurs, ces méthodes ont donné des résultats très encourageants:

Penrose (1935) applique sa méthode à 60 sibpairs examinés pour les groupes sanguins, les cheveux roux et les yeux bleus. Il ne trouve aucun linkage. *Barbara Burks* (1930) avait déjà eu l'idée d'appliquer le principe de la comparaison des paires à 16 000 familles étudiées en 25 ans par l'Eugenic Record Office. (1938). Elle découvrit ainsi un linkage entre la couleur des cheveux et certaines anomalies dentaires, et entre la couleur des yeux et la myopie. *Halpern* (1939) examine 23 familles pour les tests psychologiques de *Binet-Termann* sans trouver de relation entre le sexe et les aptitudes. *Burks* et *Wyand* (1941) examinant 24 familles (14 paires) ne trouvent aucun lien entre les groupes sanguins et l'ovalocytose. *Rife* (1941) trouve un linkage entre la ligne D du 4me espace interdigital et l'habileté manuelle (droitiers) en examinant 26 familles (248 paires). Il ne trouve par contre aucun linkage pour les autres lignes de la main (*Rife* et *Klœpfer* 1943). *Snyder*, *Baxter* et *Knisely* (1941) examinent 64 familles (190 paires) pour le P.T.C. et les groupes sanguins sans trouver de linkage. *Boyd* et *Boyd* (1941) pour la première fois dans l'histoire du linkage autosomique étudient à la fois un grand nombre de caractères, soit 500 paires examinées pour 7 caractères: Sexe, groupes sanguins, poils de la deuxième phalange, P.T.C., couleur des cheveux, couleur des yeux, et couleur de la peau. *Finney* applique sa méthode à ces observations sans réussir à mettre en évidence de linkage. *Fisher* (1936) essaye aussi de découvrir un linkage entre les groupes sanguins et la maladie de *Friedreich*, mais n'obtient que des résultats discutables. Enfin, *Penrose* (1946 a et b), *Munro*, *Penrose* et *Taylor* (1939) et *Haldane* (1948) cherchent un linkage entre l'oligophrénie phenylpyruvique et les groupes ABO; dans aucun cas ils ne trouvent des chiffres vraiment significatifs [1]).

Il faut arriver au magnifique travail de *Klœpfer* (1946), auquel nous faisons de nombreux emprunts pour trouver une large application de la méthode de *Penrose*. *Klœpfer* a examiné en effet 27 familles, totalisant 903 paires pour 19 caractères, soit selon la formule n(n–1)/2, 171 possibilités de linkage.

---

[1]) Citons encore le travail de *Rywlin* (1950) qui montre par la sib-pair method qu'il n'y a pas de linkage entre la rétinite pigmentaire et les groupes sanguins ABO.

Au moyen de la méthode du 2 × 2 et de la „graded character method", et en faisant une troisième vérification par une modification de la „graded method", il trouve 16 linkages probables ou possibles, soit:

1. Décollement de l'oreille et longueur des doigts.
2. Longueur des doigts et couleur des yeux.
3. Décollement de l'oreille et couleur des yeux.
4. Surface de l'oreille et P.T.C.
5. P.T.C. et M.B.S.
6. Surface de l'oreille et M.B.S.
7. M.B.S. et Curling.
8. P.T.C. et Curling.
9. Tourbillon des cheveux et strabisme.
10. Strabisme et couleur des cheveux.
11. Tourbillon et couleur des cheveux.
12. Types sanguins et décollement de l'oreille.
13. Surface de l'oreille et décollement de l'oreille.
14. Couleur des yeux et Curling.
15. Curling et teinte des cheveux.
16. Teinte des cheveux et couleur des cheveux.

Ces résultats, des plus intéressants, ont pu être obtenus en examinant un grand nombre de caractères normaux, relativement aisés à rechercher et qui permettent de réunir un matériel suffisant pour obtenir des résultats probants.

Franceschetti a encore insisté tout récemment (1949) sur l'importance de ces caractères héréditaires anthropologiques, qu'il a nommés „marqueurs de chromosomes". Il en a publié la liste en se basant sur tous ceux qui avaient été utilisés par les divers auteurs cités et en a ajouté 4 nouveaux: L'œil directeur, les anomalies dentaires, les anomalies des ongles, et le facteur Rhésus. Il nous a alors proposé de reprendre l'étude du linkage autosomique en utilisant la méthode de *Penrose*, en examinant les paires pour le plus grand nombre possible de „marqueurs de chromosomes" et en recherchant en plus un nouveau caractère: l'œil directeur.

Recherches personnelles.

Nous avions en commençant ces recherches 3 buts principaux:

a. Vérifier les résultats de *Klœpfer* au moyen d'une série d'observations recueillies dans une population toute différente.

b. Examiner les possibilités de linkage pour un nouveau caractère: l'œil directeur.

c. Apporter un certain nombre de familles et de paires susceptibles d'être utilisées en union avec les résultats d'autres auteurs pour des vérifications et des recherches de linkage faites à une plus grande échelle.

Méthodes et Techniques.

I. *Les caractères utilisés.*

Nous avons examiné 20 familles pour 17 caractères, dont la liste et les symbôles se trouvent dans le tableau 1. Dans la mesure du possible, nous avons classé nos caractères de la même façon que *Klœpfer*, de manière à rendre nos résultats comparables aux siens.

Tableau 1. Liste des caractères étudiés et des numéros qui les représentent dans les tableaux suivants.

No.	Caractères	1	2	3	4	5
1.	PTC	positif	negatif			
2.	Longueur des doigts	annulaire	indifférent ou 2 mains inégales	index		
3.	Poils de la 2me phalange	1 doigt	2 doigts	3 doigts	4 doigts	5 doigts
4.	Handedness	droitier	gaucher			
5.	Teinte des cheveux	blonds	bruns clairs	bruns	bruns foncés	noirs
6.	Couleur des cheveux	non roux	roux			
7.	Tourbillon	droit	indifférent	gauche		
8.	Forme des cheveux	droits	frisés			
9.	Taille de l'oreille	petite	moyenne	grande		
10.	Position du pavillon de l'oreille	collé	moyen	décollé		
11.	Position du lobule de l'oreille	libre	collé			
12.	Couleur des yeux	bleus	non bleus			
13.	Strabisme	absent	présent			
14.	Oeil directeur	droit	gauche			
15.	Naevi	absents	présents			
16.	Curling	présent	absent			
17.	Sexe	garçon	fille			

1. *P.T.C.*

La sensibilité gustative à la Phenylthiocarbamide ou P.T.C. est un caractère héréditaire dont le mode de transmission a été établi par *Snyder* en 1932; la perception d'un goût étant dominante sur l'absence de toute perception.

Nous avons testé nos sujets en imbibant un fragment de papier buvard avec la solution standard, et en le posant sur la langue. Les sujets positifs perçoivent un goût amer, très intense, et désagréable. Les sujets négatifs avaient l'impression de goûter à de l'eau. Dans nos tableaux les sujets positifs sont représentés par le chiffre 1, et les négatifs par le chiffre 2.

2. *La longueur des doigts.*

C'est *Klœpfer* qui utilisa pour la première fois ce caractère. On le recherche en demandant au sujet d'étendre ses doigts le plus possible, et l'on examine la longueur relative du 2me et du 4me doigt (index et annulaire). On trouve le plus souvent que l'annulaire est plus long que l'index; parfois c'est l'index qui est plus long, et rarement les deux doigts ont une longueur égale. Dans les tableaux, les cas ayant l'annulaire plus long que l'index portent le chiffre 1, ceux qui ont les deux doigts égaux portent le chiffre 2 et ceux qui ont l'index le plus long, le chiffre 3.

3. *Les poils de la deuxième phalange.*

Ce caractère fut utilisé pour la première fois par *Burks* et *Wyandt*, puis par *Boyd* et enfin par *Klœpfer*. On le trouve facilement en examinant à la loupe la deuxième phalange de chaque doigt, et on groupe les cas en 5 classes selon la présence de follicules pileux sur, 0, 1, 2, 3, ou 4 doigts.

4. *Handedness.*

Chamberlain (1928) a mis en évidence le caractère héréditaire de l'habileté manuelle gauche ou droite (droitiers ou gauchers). *Rife* (1941) l'utilisa pour la première fois dans une étude sur le linkage, puis *Klœpfer* l'intégra dans sa série. Le diagnostic en est relativement facile; notons toutefois qu'il faut de temps à autre le concours des parents ou de l'instituteur pour avoir une certitude. La plupart de nos sujets étaient droitiers.

5. *La teinte des cheveux.*

La teinte des cheveux est probablement due à un grand nombre de gènes comme l'ont montré les études de la couleur du pelage des mammifères. On peut cependant facilement l'utiliser dans la méthode de *Penrose* qui ne nécessite pas une connaissance exacte du mode de transmission héréditaire des caractères considérés. Les résultats obtenus nous apprendront simplement que l'un ou l'autre des gènes influençant la teinte des cheveux est lié avec d'autres ou non.

Pour mesurer la teinte des cheveux, il suffit de la comparer avec une échelle standard. Nous avons utilisé celle de l'Institut d'Anthropologie de Genève, que M. le Prof. *Sauter* a bien voulu mettre à notre disposition. Comme *Klœpfer*, nous avons classé la teinte des cheveux en 5 groupes portant les numéros 1 à 5:

1. Cheveux blonds
2. Cheveux bruns clairs
3. Cheveux bruns
4. Cheveux bruns foncés
5. Cheveux noirs.

6. *La couleur des cheveux.*

Nous distinguons 2 groupes de couleurs de cheveux, les individus faisant partie de la série à cheveux roux, et les individus faisant partie de la série à cheveux blonds dont les diverses teintes ont été énumérées ci-dessus.

Sous chiffre 1 on trouvera les individus à cheveux blonds, sous chiffre 2 les individus à cheveux roux. Notons aussi toute l'incertitude qui règne encore sur le mode de transmission des cheveux roux, dont le caractère héréditaire est cependant certain.

7. *Le Tourbillon.*

Klœpfer utilise pour la première fois comme marqueur de chromosome la façon dont les cheveux s'implantent sur l'occiput (Tourbillon ou Hair whorl). Certains individus ont un tourbillon qui tourne dans le sens des aiguilles d'une montre (tourbillon droit, No. 1) et d'autres ont un tourbillon qui tourne dans le sens opposé (tourbillon gauche ou No. 3). Certains sujets ont un double tourbillon, gauche et droit, ou n'en ont pas du tout, leurs cheveux s'implantent sans ordre visible. Nous les avons classé sous le chiffre No. 2.

La recherche de ce caractère est très facile, chez l'enfant comme chez l'adulte, et n'a comme inconvénient que de déranger parfois une coiffure féminine trop bien échafaudée.

8. *La forme des cheveux.*

Klœpfer utilise aussi ce caractère dont il établit la transmission héréditaire. Il classe la forme des cheveux en 3 groupes: Cheveux droits, cheveux ondulés, et cheveux bouclés. Nous n'avons eu que peu de variations dans notre série au point de vue de ce caractère et nous nous sommes contentés de 2 groupes: Cheveux droits (No. 1) et Cheveux frisés (No. 2).

9. *La taille de l'oreille.*

C'est encore *Klœpfer* qui utilisa la taille de l'oreille pour la première fois et en fit un caractère héréditaire. Sa recherche a malheureusement le défaut d'être très subjective et de dépendre uniquement de l'impression de l'examinateur. Nous pouvons cependant confirmer pleinement les résultats de *Klœpfer*, et dire que l'estimation de la grandeur d'une oreille se fait relativement facilement, et que plusieurs examinateurs sont arrivés régulièrement dans nos séries à des résultats identiques chez un même individu.

On classe la taille de l'oreille en 3 groupes: Oreilles petites (1), moyennes (2) et grandes (3).

10. *Le décollement de l'oreille.*

La position du pavillon de l'oreille par rapport au crâne est également un caractère héréditaire mis en évidence par *Klœpfer*. On le recherche en regardant la tête par derrière et en notant la plus ou moins grande distance qui sépare le pavillon de l'oreille du crâne. Là encore le résultat dépend de l'appréciation de l'examinateur, mais les différences sont le plus souvent tellement nettes que l'on ne peut guère se tromper. On classe les oreilles en 3 groupes: oreilles collées (1), moyennes (2) et décollées (3).

11. *Le lobule de l'oreille.*

Klœpfer divise en trois groupes la façon dont le lobe de l'oreille s'attache à la peau du crâne; groupes basés sur l'angle que fait le bord du lobule avec la peau de la joue. Pratiquement nous n'avons trouvé

que deux sortes de lobules, les uns collés (No 2), les autres libres (No. 1). Aucun auteur, à notre connaissance n'a utilisé ce caractère avant *Klœpfer*.

12. *La couleur des yeux.*

Le diagnostic précis de la couleur des yeux ne peut se faire sans une table du type de celle de *B. Schultz*. Nous avons utilisé une telle table, mise à notre disposition par la Julius Klaus-Stiftung, au début de notre enquête; mais, comme *Klœpfer*, nous y avons rapidement renoncé, trouvant que l'appréciation subjective était plus facile et suffisamment précise. Nous n'avons utilisé pour les tables de *Penrose* que deux caractères: la présence (No. 1) ou l'absence (No. 2) des yeux bleus.

13. *Le strabisme.*

Nous n'avons eu que peu de variation de ce caractère dans les familles étudiées, cependant, selon *Penrose*, celà ne trouble pas l'efficacité de la méthode. Nous l'avons donc retenu, avec succès d'ailleurs, puisque nous confirmons un linkage déjà trouvé par *Klœpfer*.

Dans les tableaux, la présence du strabisme correspond au chiffre 2 et son absence au chiffre 1.

14. *L'œil directeur.*

Ce caractère n'a pas encore été utilisé dans les études sur le linkage, et sa transmission génétique est encore à établir. C'est sur la proposition du Prof. *Franceschetti* que nous l'avons inclu à notre série. Voici comment on le recherche:

„La personne à examiner tient un objet allongé (p.e. un crayon), le bras bien étendu; elle doit essayer de couvrir l'œil droit de l'observateur qui se tient à une certaine distance, l'œil gauche étant fermé. L'œil fixateur se trouve alors dans la prolongation de l'œil de l'observateur par l'objet qui est tenu dans sa direction (*Franceschetti*)".

On groupe les sujets en 2 classes: ceux qui ont l'œil directeur droit (No. 1) et ceux qui ont l'œil directeur gauche (No. 2).

15. *Naevi.*

La présence de naevi est assez rare dans notre série, et nous ne pouvons attribuer que très peu de crédit aux résultats obtenus avec ce caractère. Dans les tableaux, la présence de naevi porte le chiffre 2, l'absence le chiffre 1.

16. *Le Curling (Enroulement de la langue).*

C'est encore *Klœpfer* qui utilise pour la première fois ce test dans une étude sur le linkage Il classe ses sujets en 3 groupes: Ceux qui peuvent relever les bords de leur langue suffisamment pour la transformer en un véritable tube fermé; ceux qui peuvent les relever seulement pour en faire un sorte de gouttière, et ceux qui ne peuvent pas du tout les relever.

Nous avons classé nos sujets en 2 groupes seulement, les Curling + (No. 1) qui correspondent au groupe 1 et 2 de *Klœpfer*, et les Curling — (No. 2) qui correspondent au troisième groupe de *Klœpfer*.

17. *Le sexe.*

No. 1 pour les garçons et No. 2 pour les filles.

Les conditions de notre enquête ne nous ont pas permis de rechercher les facteurs Rhésus, ni la sensibilité gustative au M.B.S (Mercaptobenzoselenazol). Quant aux anomalies des dents et des ongles, nous n'en avons rencontré qu'une seule, ce qui ne permet pas d'en tenir compte.

Nous avons examiné 20 familles prises au hasard de la population genevoise, les unes examinées dans une école de campagne, les autres à domicile. Dans la plupart des cas les parents acceptèrent facilement de laisser examiner leurs enfants; nous rencontrâmes plus de difficultés pour les examens scolaires, où les démarches auprès des autorités pourtant très compréhensives, prennent beaucoup de temps, et où, l'intransigeance de certains parents rend l'examen de quelques familles impossible. Aussi, la plupart des familles examinées furent elles repérées lors de l'admission d'un de leurs membres à l'hôpital, les autres membres étant examinés à domicile. L'organisation sociale de l'enquête et le dépistage des familles nombreuses constituent certainement la partie la plus longue et la plus difficile de ces recherches. Tout le reste est relativement vite fait lorsque toutes les observations sont réunies.

II. *La Méthode du 2 × 2 de Penrose.*

Le principe et la démonstration de la méthode de *Penrose* ont été exposés par *Penrose* en 1935 et par *Franceschetti* en 1949. Nous n'y reviendrons pas. Rappelons cependant qu'il consiste à comparer entre eux des paires de frères et sœurs (sibpairs) pour deux caractères considérés. Si, par exemple, nous étudions la possibilité d'un linkage

Tableau 2. Distribution des paires selon la concordance ou la discordance pour le décollement du pavillon de l'oreille et le lobule de l'oreille.

Fam. No.	CC	CD	DC	DD	Nombre de paires
1	3			3	6
2	1	1	2	2	6
3	3		3		6
4	3			3	6
5	3			3	6
6	3		3		6
7	3		3		6
8	3		3		6
9	2		4		6
10	1	2	2	1	6
11	2		4		6
12	4	6	3	2	15
13	6			4	10
14	1	1	4	4	10
15		2	3	5	10
16	6		4		10
17	6	4	1	4	15
18	6	4			10
19	10				10
20	4		6	5	15
	70	20	45	36	171
	a	b	c	d	

Tableau pour le calcul du χ^2.

		Décollement de l'oreille C	D	Total
Lobule de l'oreille	C	a (70)	b (20)	90 (a+b)
	D	c (45)	d (36)	81 (c+d)
	Total	115 (a+c)	56 (b+d)	171 (n)

$$\chi^2 = \frac{n\,(ad - bc)^2}{(a+b)\,(c+d)\,(a+c)\,(b+d)} = \frac{171\,(70 \,.\, 36 - 20 \,.\, 45)^2}{90 \,.\, 81 \,.\, 56 \cdot 115} = 9{,}55^{**}$$

probabilité: 0,001.

entre l'œil directeur et le Curling, nous pourrons grouper toutes les paires selon 4 possibilités:

a. Une première possibilité où les deux sujets comparés sont semblables pour l'œil directeur et le Curling; l'un et l'autre étant, par

Tableau 3. Distribution des paires selon la concordance et la discordance pour l'œil directeur et le curling.

Fam. No.	CC	CD	DC	DD	Nombre de paires
1	3		3		6
2	3	3			6
3	2	4			6
4	2	4			6
5	3	3			6
6	3		3		6
7	6				6
8	6				6
9	2	4			6
10	3			3	6
11	1	2	1	2	6
12	6	1	4	4	15
13	4	6			10
14	1	3	3	3	10
15	4	6			10
16	3	1	3	3	10
17	10		5		15
18	10				10
19	3	1	3	3	10
20	2	5	4	4	15
	77	43	29	22	171

Tableau pour le calcul du χ^2.

		Oeil directeur		
		C	D	Total
Curling	C	77	43	120
	D	29	22	51
	Total	106	65	171

$$\chi^2 = \frac{171 \,.\, (77 \,.\, 22 - 43 \,.\, 29)^2}{120 \,.\, 51 \,.\, 106 \,.\, 65.} = 0{,}8103. \qquad \text{probabilité: } 0{,}18.$$

exemple, Curling + et ayant un œil directeur droit. Ils sont dits concordants pour les deux caractères (C.C.).

b. Une seconde possibilité où les deux sujets sont concordants pour le premier caractère (ils ont, par exemple, tous les deux un œil

directeur gauche) et discordants pour le second caractère (l'un étant Curling + et l'autre Curling —). Ils sont dits Concordants-Discordants (C.D.).

c. Une troisième possibilité où les deux sujets sont discordants pour le premier caractère (l'un ayant l'œil directeur gauche et l'autre droit) et concordants pour le second (tous les deux sont, par exemple, Curling —). Ils sont dits Discordants–Concordants (D.C.).

d. Enfin une dernière possibilité où les 2 sujets sont discordants pour les deux caractères. (l'un étant Curling + et ayant un œil directeur droit, alors que l'autre est Curling — et a un œil directeur gauche). Ils sont discordants pour les deux caractères (D.D.).

En faisant ces comparaisons dans chaque famille, et en y considérant toutes les paires de frères et sœurs, comparant chacun avec tous les autres, nous obtiendrons 4 groupes de paires que nous pourrons disposer dans un grand tableau (Tab. 2 et 3).

On fait ensuite le total de chacune des possibilités (CC, CD, DC et DD). Le nombre de paires pour une famille donnée est obtenu par la formule suivante:

$$\text{nombre de paires} = n\,(n - 1)\,/\,2.$$

Ou n représente le nombre des frères et sœurs (sibship). Ainsi pour une famille de 5 enfants on aura:

$$5\,(5 - 1)\,/\,2 = 10 \text{ sibpairs.}$$

On peut suspecter un linkage si le produit des paires CC . DD est plus grand que le produit des paires CD . DC. Pour savoir si la différence des deux produits n'est pas uniquement due au hasard, *Penrose* applique la méthode dite du χ^2. On dispose les totaux de chaque colonne du tableau groupant les sibpairs par groupes de 2 sur un nouveau tableau, et l'on calcule la valeur de χ^2 en utilisant la formule suivante:

$$\chi^2 = \frac{n \cdot (a \cdot d - b \cdot c)^2}{(a + b)\,(c + d)\,(a + c)\,(b + d)}$$

Les tableaux 2 et 3 donnant un exemple pour les caractères position du pavillon de l'oreille et lobule de l'oreille, et pour l'œil directeur et le Curling.

Un χ^2 de 3,84 signifie qu'il n'y a que 5 % de chances que la différence entre les deux produits CC . DD et CD . DC soit due au hasard. Un χ^2 de 6,63 signifie qu'il n'y a que 1 % de chances que la différence soit due au hasard. Autrement dit, dans tous les cas ou le χ^2 aura une valeur entre 3,84 et 6,63 nous pourrons dire que le linkage entre les deux caractères considérés est possible, et que dans tous les cas ou le χ^2 se trouve au dessus de 6,63 le linkage entre ces deux caractères est très probable. Ainsi, comme on le voit dans le tableau 2, le linkage entre le décollement et le lobule de l'oreille est probable, le χ^2 ayant une valeur de 9,55. Par contre, comme le montre le tableau 3, le χ^2 pour le linkage entre l'œil directeur et le Curling est de 0,810, soit nettement trop bas. Il y a donc pas de linkage entre ces deux caractères.

Notons enfin et surtout les grands avantages de la méthode de *Penrose*, qui n'a besoin ni de la connaissance exacte du mode de transmission héréditaire des caractères considérés, ni de l'examen des parents dans les familles étudiées.

III. *La méthode du 3 × 3 de Penrose.*

Pour vérifier certains résultats obtenus, nous avons tenté de leur appliquer la méthode de 3 × 3 (*Penrose* 1940). Cette méthode repose sur les mêmes principes que celle du 2 × 2, mais donne une précision $6^1/_4$ fois plus grande. Au lieu de comparer seulement les paires concordantes et discordantes pour deux caractères donnés, on note encore de quelle façon il y a concordance et discordance. Si l'on considère chez deux sujets, deux caractères A et P et leurs allèles B et Q, nous pouvons les grouper selon 9 possibilités:

AA PP	AB PP	BB PP
AA PQ	AB PQ	BB PQ
AA QQ	AB QQ	BB QQ

Comme pour la méthode du 2 × 2, on examine chaque paire et on les classe dans la colonne du groupe auquel elles correspondent. On fait le total de chacune des colonnes et on dispose les résultats sur un tableau, mais en les groupant cette fois par groupes de 3. On calcule alors la valeur du χ^2 comme pour la méthode du 2 × 2; seulement les chiffres significatifs seront de 9.48 pour une probabilité de 5 % et de 13.27 pour une probabilité de 1 %.

Malheureusement, la méthode du 3 × 3 n'est applicable que lorsque l'on considère des caractères ne présentant que 2 états (positifs et négatifs) sans moyen terme. Dans notre série, nous ne pûmes appliquer le 3 × 3 que dans 6 cas. Le tableau 4 en est un exemple [1]).

Les résultats.

Le tableau 5 donne les valeurs de χ^2 pour les 132 possibilités de linkage étudiées par la méthode du 2 × 2. Nous y trouvons 16 possibilités ou probabilités de linkage réunies dans le tableau 6. Certains chiffres placés entre parenthèse, bien que significatifs, ne peuvent être retenus, car dans ces cas, les cases b et c du tableau du 2 × 2 contenaient des nombres trop grands, et le χ^2 significatif obtenu pouvait être dû au hasard ou à toute autre condition sans aucun rapport avec le linkage.

---

[1]) Les calculs des χ^2 ont été executés par M. *A. A. Weber* du Laboratoire de Statistique Mathématique de l'Université de Genève (Directeur: Prof. *A. Linder*) auquel nous exprimons toute notre reconnaissance. Nos remerciements vont aussi au Prof. *Linder* qui a bien voulu contrôler l'interprétation mathématique de nos résultats.

ableau 4. Distribution des paires pour le PTC et la position du lobule de l'oreille en vue de l'établissement du linkage par la méthode du 3 × 3.

Fam. No.	AA/PP	AA/PQ	AA/QQ	AB/PP	AB/PQ	AB/QQ	BB/PP	BB/PQ	BB/QQ	Nombre de paires
1	1	2		2	1					6
2	3	3								6
3	3			3						6
4	3				3					6
5		3	3							6
6		3	3			3				6
7							6			6
8	6									6
9			6							6
10	1			2	2			1		6
11	3			3						6
12	6	8	1							15
13								4	6	10
14	1	6	3							10
15				4			6			10
16	1	6	3							10
17	6	8	1							15
18	3	3		3	1					10
19	10									10
20	3			6	3		1	2		15
	50	39	20	23	10	3	13	7	6	171

		P.T.C.			
		AA	AB	BB	Total
Lobule de l'oreille	PP	50	23	13	86
	PQ	39	10	7	56
	QQ	20	3	6	29
	Total	109	36	26	171

$$\chi^2 = 5{,}15$$

Les valeurs du χ^2 dans notre série et dans celle de *Klœpfer* sont comparées dans le tableau 7. Pour 4 linkages, soit

Taille de l'oreille – décollement de l'oreille

Lobule de l'oreille – longueur des doigts

Taille de l'oreille – P.T.C.

Strabisme – Couleurs des cheveux.

nous confirmons les résultats de *Klœpfer*. Pour 12 autres linkages, nous trouvons des chiffres significatifs, alors que *Klœpfer* n'en trouve pas, et pour 12 autres linkages découverts par *Klœpfer* nous trouvons des χ^2 en dessous du seuil significatif.

Il est difficile d'expliquer ces différences. S'agit il d'une question de race? de population étudiée? S'agit il du nombre des familles? du nombre des paires? Il n'est pas facile de prendre position. Nous pensons cependant que ces contradictions sont inhérentes à l'application de toute méthode nouvelle; que les résultats obtenus, ceux de *Klœpfer* comme les nôtres, ont besoin de nombreuses vérifications par des travaux portant sur des populations très différentes; et que plus nous aurons de séries, plus les résultats concorderont.

Ces remarques s'appliquent aussi aux chiffres obtenus par la méthode du 3×3, et réunis dans le tableau 8. Nous avons appliqué cette méthode à 5 linkages de notre série, et pour aucun d'entre eux nous n'avons trouvé de χ^2 significatif. Mais, comme le montre le tableau 4, le total de plusieurs colonnes ne compte qu'un chiffre très faible; dans d'autres tableaux on trouve plusieurs 0. Les χ^2 calculés avec ces nombres n'ont qu'une signification bien faible et ne peuvent être retenus.

Pour augmenter la variation des caractères et accroître leur dispersion, nous avons essayé de combiner notre série à celle de *Klœpfer* et de calculer la valeur du χ^2 par la méthode du 3×3 pour les deux séries réunies. Deux linkages, lobule de l'oreille – P.T.C. et couleur des cheveux – strabisme, nous ont donné des valeurs significatives. Cependant, là encore, il faut accepter ces chiffres avec réserve, car les deux séries diffèrent entre elles.

Ces résultats viennent donc à l'appui des conclusions qui se dégagent de l'application de la méthode du 2×2, c'est à dire la nécescité de poursuivre les examens de nombreuses familles dans les populations différentes; de grouper les résultats, et seulement alors de calculer les valeurs de χ^2, valeurs qui prendront une signification beaucoup plus complète.

Il reste malgré toutes ces réserves un fait très encourageant, c'est que les linkages obtenus le sont tous entre des caractères voisins, ayant déjà certaines liaisons connues.

Les tableaux 9 et 10 qui groupent en un schéma tous les linkages autosomaux connus, montrent qu'il se dessine 2 ou 3 grands groupes de caractères liés entre eux. Nos résultats apportent de nou-

Tableau 5. Valeur des χ^2 obtenus par la méthode du 2 × 2 pour 136 possibilités de linkage.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
17	0,59	0,24	0,06	2,18	0,33	*0,05*	0,28	2,36	0,12	3,05	1,05	0,08	0,00	0,31	1,40	0,14
16	0,98	0,05	0,72	0,52	2,50	*0,12*	2,39	0,84	**2,13**	3,51	0,01	0,05	0,00	0,81	3,37	
15	*0,08*	*0,54*	0,62	*0,17*	*0,07*	*0,32*	*0,32*	*0,64*	0,33	0,54	*0,21*	0,71	*0,29*	1,29		
14	1,82	1,50	1,71	2,96	0,17	*0,34*	**9,81**	**6,85**	0,02	0,06	0,06	0 62	1,68			
13	0,18	1,44	0,00	*0,61*	(5,27)	**3,74**	*0,39*	*0,05*	0,24	0,00	1,06	0,02				
12	2,48	2,58	**8,04**	**4,45**	0,08	*0,60*	0,00	1,88	0,25	1,39	0,01					
11	**4,13**	**8,19**	0,00	**5,37**	0,38	*0,51*	0,86	0,70	**6,21**	**9,55**						
10	2,88	0 08	3,20	3,38	1,08	1,79	0,09	0,08	**17,5**							
9	**11,1**	1,08	3,60	(6,63)	0,11	3,03	2,55	0,01								
8	**4,33**	0,02	0,74	1,00	0,66	*0,18*	*0,36*									
7	0,02	**4,39**	0,05	0,11	2,64	*0,23*										
6	*0,61*	*0,41*	*0,28*	*0,71*	–,—											
5	1,16	2,86	3,81	0,56												
4	1,74	**6,02**	1,02													
3	0,03	(4,75)														
2	0,62															

Les chiffres italiques expriment la probabilité calculée par une autre méthode que celle du χ^2.
Les chiffres placés entre parenthèses n'indiquent pas un linkage.
Les chiffres gras sont significatifs pour l'établissement d'un linkage.

Tableau 6. Valeur des χ^2 significatifs indiquant un linkage.

1.	Position du pavillon de l'oreille et surface de l'oreille	17,05
2.	Position du pavillon de l'oreille et lobule de l'oreille	9,55
3.	Longueur des doigts et lobule de l'oreille	8,19
4.	Longueur des doigts et tourbillon	4,39
5.	Longueur des doigts et Handedness	6,04
6.	Surface de l'oreille et P.T.C.	11,12
7.	Surface de l'oreille et Curling	21,30
8.	Surface de l'oreille et lobule de l'oreille	6,21
9.	P.T.C. et lobule de l'oreille	4,13
10.	P.T.C. et forme des cheveux	4,33
11.	Cheveux roux et strabisme	3,74
12.	Oeil directeur et forme des cheveux	6,85
13.	Oeil directeur et tourbillon	9,81
14.	Handedness et lobule de l'oreille	5,37
15.	Handedness et couleur des yeux	4,45
16.	Couleur des yeux et poils de la 2me phalange	8,04

Tableau 7. Valeur comparée des χ^2 significatifs de notre série et de celle de *Klœpfer.*

	Klœpfer	*Taillard*
Pavillon de l'oreille – Longueur des doigts	10,70	0,031
Pavillon de l'oreille – Couleur des yeux	47,20	2,58
Pavillon de l'oreille – Surface de l'oreille	3,58	17,05
Pavillon de l'oreille – Lobule de l'oreille	0,03	9,55
Longueur des doigts – Couleur des yeux	4,04	2,58
Longueur des doigts – Lobule de l'oreille	10,0	8,19
Longueur des doigts – Tourbillon	0,88	4,39
Longueur des doigts – Handedness	0,06	6,04
Surface de l'oreille – P.T.C.	23,01	11,12
Surface de l'oreille – Curling	0,59	21,30
Surface de l'oreille – Curling	0,59	21,30
Surface de l'oreille – Lobule de l'oreille	1,81	6,21
P.T.C. et Curling	5,4	0,93
P.T.C. et lobule de l'oreille	(7,4)	4,13
PTC et forme des cheveux	0,07	4,33
Cheveux roux et strabisme	11,26	3,74
Cheveux roux et teinte des cheveux	6,70	—
Cheveux roux et tourbillon	14,10	0,23
Teinte des cheveux et Curling	0,66	2,50
Curling et couleur des yeux	14,26	2,50
Tourbillon et strabisme	4,76	0,39
Handedness et lobule de l'oreille	0,00	5,37
Handedness et couleur des yeux	0,05	4,45
Couleur des yeux – Poils de la 2me phalange	0,04	8,04

Tableau 8. Valeur des χ^2 obtenus par la méthode du 2×2 et du 3×3 avec nos séries et celles de *Klœpfer*.

	1	2	3	4
Forme des cheveux – PTC	4,33	0,07	8,91	
Forme des cheveux et œil directeur	6,85		7,03	
P.T.C. et lobule de l'oreille	4,13	7,4	5,15	17,57
Lobule de l'oreille et handedness	5,37	0,00	4,30	
Handedness et couleur des yeux	4,45	0,05	7,63	
Couleur des cheveux et strabisme	3,74	11,26		13,27

Col. 1: χ^2 obtenus par la méthode du 2×2 dans notre série. Col. 2: χ^2 obtenus par la méthode du 2×2 dans la série de *Klœpfer*. Col. 3: χ^2 obtenus par la méthode du 3×3 dans notre série. Col. 4: χ^2 obtenus par la méthode du 3×3 dans notre série réunie à celle de *Klœpfer*.

Tableau 9. Liste des linkages autosomiques actuellement connus chez l'homme.

1. Position du pavillon de l'oreille et longueur des doigts
2. — et couleur des yeux
3. — et type sanguin
4. — et surface de l'oreille
5. — et lobule de l'oreille
6. Longueur des doigts et couleur des yeux
7. — et lobule de l'oreille
8. — et tourbillon
9. — et Handedness
10. Surface de l'oreille et P.T.C.
11. — et M.B.S.
12. — et Curling
13. — et lobule de l'oreille
14. P.T.C. et M.B.S.
15. P.T.C. et Curling
16. P.T.C. et forme des cheveux
17. M.B.S. et Curling
18. Cheveux roux et strabisme
19. — et teinte des cheveux
20. — et tourbillon
21. Curling et teinte des cheveux
22. — et couleur des yeux
23. Oeil directeur et forme des cheveux
24. — et tourbillon
25. Tourbillon et Strabisme
26. Couleur des yeux et Myopie (*Burks*)
27. — et poils de la 2me phalange
28. — et Handedness
29. Lobule de l'oreille et Handedness

30. Lobule de l'oreille et P.T.C.
31. Lignes de la main et Handedness (*Rife*)
32. Couleur des cheveux et anomalies des dents (*Burks*)
33. Type sanguin et anémie à hématies falciformes (*Snyder*)
34. Groupes sanguins et allergie (*Finney*).

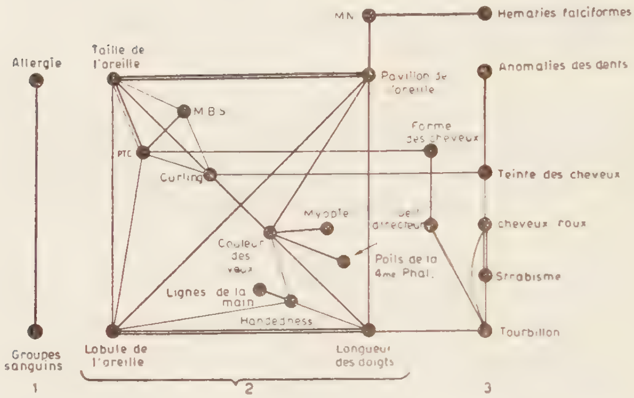


Tableau 10. Schéma des linkages autosomiques actuellement connus. ═══ Linkages mis en évidence dans la série de *Klœpfer* et dans la nôtre. Ces linkages peuvent être considérés comme certains. ▬▬▬ Linkages probables. ——— Linkages possibles. 1 – 2 – 3 Groupes de caractères qui pourraient correspondre à une même paire de chromosomes.

velles possibilités de linkage à l'intérieur de ces grands groupes, faisant en quelques sortes une série de recoupements entre des caractères montrant une grande tendance à l'association et laissant prévoir qu'ils se trouvent peut être sur une même paire de chromosome.

C'est en poursuivant ces recherches, que l'on obtiendra, nous l'espérons, d'autres recoupements à l'intérieur des mêmes groupes, et que nous pourrons commencer une carte chromosomique précise, comme celle que l'on pût dessiner chez la Drosophile. Nous ne pouvons nous empêcher de faire un rapprochement entre l'état actuel des recherches sur le linkage humain et les débuts des recherches sur le linkage en génétique expérimentale, alors qu'il n'existait que quelques travaux aux résultats incertains et discutés, travaux autour desquels vinrent se grouper une pléiade de vérifications qui aboutirent aux brilliantes et précises conclusions que l'on connaît. Pour l'instant, nous ne pouvons qu'émettre quelques hypothèses hasardeuses et souhaiter que nos résultats soient le plus vite possible vérifiés et complétés.

Notons cependant les remarques de *J. W. Neel* (1948) sur l'intérêt pratique du linkage en génétique humaine. Cet auteur montre que le linkage aura vraisemblablement un champ d'application restreint tout au moins dans le domaine de la recherche des porteurs de gènes et dans l'établissement du pronostic héréditaire de certaines affections.

Ces critiques mettent bien en évidence les difficultés que l'on rencontre lorsque l'on veut appliquer à des cas bien déterminés les méthodes statistiques. Il en est du linkage comme pour tous les problèmes de génétique humaine; nous ne parlons que de probabilité et de hasard. Mais nous n'en croyons pas moins que le linkage mérite d'occuper une grande place en génétique humaine comme en génétique expérimentale et qu'il nous apportera, sinon des résultats pratiques immédiats, du moins des démonstrations théoriques des plus précieuses.

Résumé et conclusions.

Nous avons examiné 20 familles soit 171 sibpairs, pour 17 caractères héréditaires, soit 132 possibilités de linkage. Nous avons trouvé par la méthode du 2 × 2 de *Penrose* 16 linkages soit:

a. 4 linkages déjà mis en évidence par *Klœpfer* et dont les χ^2 sont hautement significatifs.
ce sont:
1. Taille de l'oreille et décollement de l'oreille.
2. Lobule de l'oreille et longueur des doigts.
3. Taille de l'oreille et P.T.C.
4. Cheveux roux et strabisme.

b. 5 linkages pour lesquels le χ^2 a une valeur hautement significative (> 6,63). Ce sont:
1. Décollement de l'oreille et lobule de l'oreille.
2. Surface de l'oreille et Curling.
3. Oeil directeur et Forme des cheveux.
4. Oeil directeur et tourbillon.
5. Couleur des yeux et poils de la 2me phalange.

c. 7 linkages pour lesquels la valeur de χ^2 est significative (> 3,84).
Ce sont:
1. Longueur des doigts et tourbillon.
2. Longueur des doigts et handedness.
3. Surface et lobule de l'oreille.
4. P.T.C. et lobule de l'oreille.

5. P.T.C. et forme des cheveux.
6. Lobule de l'oreille et handedness.
7. Handedness et couleur des yeux.

Nous pouvons donc considérer comme certains les 4 linkages que nous avons mis en évidence avec *Klœpfer*; comme probables les linkages ayant une valeur significative du χ^2, et comme possibles les linkages du dernier groupe.

Nous devons également insister une fois de plus sur le caractère incertain des méthodes utilisées, et proposons d'orienter les recherches futures en tenant compte des principes suivants:

1. Recueillir le plus grand nombre possible de faits en examinant des familles nombreuses dans des populations différentes.
2. Augmenter le nombre des caractères susceptibles d'être utilisés comme marqueurs de chromosomes.
3. Normaliser les modes d'examen des différents caractères de façon à rendre les résultats comparables et à permettre la réunion des séries.
4. Grouper les observations de tous les auteurs de façon à obtenir des séries suffisantes pour que l'application des méthodes statistiques se fasse avec une précision convenable.

Tout celà demandera un travail en équipe, où mathématiciens et médecins, anthropologistes et généticiens devront travailler de concert. De cette façon, nous pouvons espérer parvenir à une connaissance plus complète et plus sûre du linkage chez l'homme, à établir une carte chromosomique, et ensuite à appliquer ces notions à la pathologie, ce qui ouvrira à l'eugénique de nombreux horizons inconnus.

Annexe.

Les tables suivantes donnent les résultats de l'examen des membres de 20 familles groupées selon le nombre des frères et sœurs.

Chaque colonne représente un caractère correspondant au chiffre figurant en tête de celle-ci. Chaque ligne représente l'ensemble de tous les caractères pour un individu, chaque chiffre figurant la qualité du caractère attribué à cet individu.

La clef des caractères et des chiffres qui les représentent se trouve dans le tableau No. 1.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
								Famille 1.								
2	2	1	1	4	1	1	1	2	3	1	2	1	2	1	1	1
1	2	3	1	3	1	1	1	2	2	2	2	1	1	1	1	2
1	3	1	1	3	1	1	1	1	3	1	2	1	1	1	1	2
1	3	3	1	4	1	1	1	1	3	1	2	1	1	2	1	2
								Famille 2.								
1	1	3	1	3	1	1	2	2	1	1	2	1	1	2	2	2
1	1	4	1	3	1	1	1	1	3	2	2	1	1	2	1	1
1	1	4	1	5	1	1	1	2	1	1	2	2	1	2	2	1
1	1	4	1	5	1	1	2	2	3	1	2	1	1	2	2	2
								Famille 3.								
1	1	3	1	3	1	1	1	1	3	1	2	1	2	1	1	1
1	1	3	1	1	1	1	1	2	2	1	2	1	2	1	2	2
2	1	3	1	2	1	1	1	2	3	1	1	1	2	1	2	1
1	2	3	1	2	1	1	1	1	3	1	2	1	2	1	1	2
								Famille 4.								
1	1	1	1	3	1	1	1	3	3	1	2	2	1	2	2	1
2	1	1	1	3	1	2	2	1	1	2	2	1	1	2	1	2
1	1	1	1	3	1	2	1	3	3	1	1	1	1	1	1	2
1	1	1	1	3	1	2	1	3	3	1	1	1	1	2	2	1
								Famille 5.								
1	1	2	1	3	1	1	1	2	1	2	2	1	2	1	1	1
1	1	2	1	R	2	3	1	3	2	1	1	2	2	1	1	2
1	1	2	1	2	1	1	1	2	1	2	1	1	2	1	1	1
1	1	1	1	2	1	1	2	2	1	2	2	2	2	1	2	1
								Famille 6.								
1	3	1	1	3	1	1	1	3	3	2	2	1	1	1	1	1
1	1	1	1	3	1	2	1	3	2	2	2	1	2	1	1	1
1	3	1	1	3	1	1	1	1	1	2	2	1	1	1	1	1
2	1	1	1	4	1	1	2	2	2	2	2	1	1	1	1	2
								Famille 7.								
2	1	1	1	3	1	1	1	3	3	1	2	2	1	1	2	1
2	2	1	1	4	1	1	1	3	3	1	2	1	1	1	2	1
2	2	1	1	4	1	2	1	2	2	1	2	1	1	1	2	2
2	1	1	1	3	1	1	1	3	3	1	2	1	1	1	2	1
								Famille 8.								
1	2	3	1	4	1	1	1	2	3	1	2	1	2	1	1	1
1	2	3	1	4	1	1	1	2	3	1	2	1	2	1	1	1
1	1	3	1	4	1	1	1	2	3	1	2	1	2	1	1	1
1	1	3	1	3	1	1	1	2	2	1	2	1	2	1	1	2

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Famille 9.																
1	1	1	1	3	1	1	1	1	1	2	1	1	2	1	2	2
1	2	1	1	2	1	1	1	1	1	2	1	1	2	1	2	2
1	2	2	1	4	1	1	1	2	2	2	2	1	2	2	1	2
1	2	2	1	4	1	1	1	2	2	2	2	1	2	2	1	2
Famille 10.																
1	1	3	1	2	1	2	1	3	3	1	2	1	2	1	2	2
2	1	3	2	4	1	2	1	3	3	1	2	1	2	1	2	2
2	1	2	1	4	1	2	1	3	3	2	2	1	2	1	2	2
1	1	2	1	4	1	2	1	1	1	1	2	1	1	1	1	2
Famille 11.																
1	3	1	1	3	1	1	1	3	3	1	2	1	2	1	2	1
2	3	3	1	3	1	1	1	3	3	1	2	1	2	1	2	1
1	1	3	2	3	1	1	1	1	1	1	2	1	1	1	1	2
1	1	3	1	3	1	1	1	1	1	1	2	1	2	1	1	2
Famille 12.																
1	1	2	1	3	1	1	1	1	2	1	2	1	2	1	2	1
1	1	4	1	3	1	1	2	2	2	1	1	1	1	1	2	2
1	1	4	1	4	1	1	2	1	2	2	2	1	1	1	2	2
1	1	4	1	4	1	1	2	1	1	1	1	1	1	1	2	2
1	1	2	1	5	1	1	2	2	2	2	2	1	1	1	2	1
1	1	2	1	4	1	4	1	2	2	1	2	1	2	1	1	1
Famille 13.																
2	1	1	1	1	1	1	1	1	2	2	1	1	1	1	1	1
1	2	3	1	3	1	1	1	1	2	2	2	1	1	1	2	1
2	2	3	1	3	1	1	1	1	1	1	2	1	1	1	2	2
2	3	3	1	4	1	1	1	2	2	2	2	1	1	1	1	1
2	1	3	1	1	1	1	1	1	2	2	2	1	1	1	1	2
Famille 14.																
1	1	2	1	4	1	1	1	3	2	2	2	1	1	1	1	2
1	1	2	1	4	1	2	1	2	1	2	2	1	1	1	2	2
1	1	2	1	4	1	1	1	3	3	1	2	1	1	1	1	1
1	1	3	2	4	1	1	1	3	2	1	2	1	2	1	1	2
1	1	2	1	4	1	2	1	1	3	2	2	1	2	1	2	1
Famille 15.																
1	1	3	1	4	1	1	1	3	2	1	2	2	2	1	2	1
2	1	1	1	4	1	1	1	2	3	1	2	1	2	1	2	1
2	1	4	1	4	1	1	1	2	3	1	1	1	2	1	1	2
2	1	4	1	4	1	1	1	2	3	1	1	1	2	1	2	1
2	1	1	1	4	1	1	1	2	3	1	2	1	2	1	1	1

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Famille 16.																
1	1	1	1	1	1	1	1	2	3	1	1	1	1	1	1	2
1	1	1	1	2	1	1	1	2	3	2	1	1	1	1	1	1
1	1	3	1	2	1	1	1	1	1	2	2	1	2	1	2	1
1	1	2	2	3	1	1	1	2	2	2	2	2	1	1	1	1
1	1	2	1	3	1	1	1	2	2	1	2	1	2	1	1	1
Famille 17.																
1	1	1	1	3	1	1	1	1	1	2	2	1	1	1	1	1
1	1	1	1	3	1	1	1	1	2	1	1	1	2	1	1	1
1	2	1	1	3	1	1	1	1	2	1	2	1	1	1	1	1
1	1	1	1	4	1	1	1	1	2	2	2	1	1	1	1	2
1	1	2	1	4	1	1	1	2	2	1	2	1	1	1	1	1
1	1	2	1	2	1	1	1	1	2	1	1	1	1	1	1	2
Famille 18.																
1	1	1	1	2	1	1	1	2	2	2	2	1	1	1	1	1
2	1	3	1	2	1	1	1	1	2	1	2	1	1	1	1	1
1	1	1	1	R	2	1	1	2	2	1	2	1	1	1	1	1
1	1	1	1	3	1	1	1	2	2	1	2	1	1	1	1	1
1	1	1	1	R	2	1	1	2	2	1	2	1	1	1	1	1
Famille 19.																
1	2	2	1	3	1	3	1	2	3	1	2	1	2	1	1	1
1	2	3	1	3	1	3	1	2	3	1	2	2	2	1	2	1
1	1	2	1	4	1	3	2	2	3	1	2	1	1	1	2	2
1	1	3	1	4	1	3	2	2	3	1	2	2	1	1	2	1
1	1	3	1	R	2	3	1	3	3	1	2	1	1	1	2	2
Famille 20.																
1	1	1	1	1	1	1	1	2	3	1	2	1	1	1	2	1
2	1	3	1	3	1	1	1	1	1	2	2	1	2	1	2	2
2	1	1	2	4	1	1	1	2	2	1	2	1	2	2	1	2
1	1	3	2	3	1	2	1	2	3	1	2	1	2	1	1	2
1	1	1	1	4	1	2	2	2	2	1	2	1	1	1	1	2
2	1	1	1	4	1	2	1	2	2	1	2	1	2	1	2	1

Summary.

Following the work of *Klœpfer*, we have used the method of *Penrose* to determine the possibilities of linkage of 17 hereditary traits considered as chromosome markers. We have, thus, examined 20 families of from 4 to 6 children, i. e. 171 sibpairs. Among the 132 possible linkages, we have determined the following 16:

1. Four linkages, already described by *Klœpfer*, which may be considered as certain: Ear size and ear flare; ear lobe and finger length; ear size an P.T.C.; red hair and strabismus.

2. Five linkages showing a very high χ^2-probability: Ear flare and ear lobe; ear size and curling; the directing eye and hair form; directing eye and hair whorl; eye colour and mid-digital hairs.

3. Seven linkages for which the χ^2 is only suggestive for linkage: finger length and hair whorl; finger length and handedness; ear size and ear lobe; P.T.C. and ear lobe; P.T.C. and hair form; ear lobe and handedness; handedness and eye colour.

As a new chromosome marker was introduced the directing eye and we could obtain evidence of two probable linkages, i. e. with hair form and hair whorl.

Zusammenfassung.

Analog dem Vorgehen *Klœpfers* haben wir vermittels der *Penrose*-Methode versucht, bei 17 Erbmerkmalen, die als „Chromosomen-Markierungsmerkmale“ angesehen werden können, Koppelungsverhältnisse zu bestimmen. Es wurden 20 Familien mit je 4 bis 6 Kindern, insgesamt 171 Geschwisterpaare untersucht. Von 132 Koppelungsmöglichkeiten konnten die folgenden 16 bestimmt werden:

1. 4 Koppelungen, die bereits von *Klœpfer* festgestellt wurden, und die als sicher angesehen werden können, nämlich zwischen: Ohrlänge und Ohrabstand, Ohrläppchen und Fingerlänge, Ohrlänge und P.T.C., Rothaarigkeit und Strabismus.

2. 5 Koppelungen auf Grund einer hohen χ^2-Wahrscheinlichkeit: Ohrabstand und Ohrläppchen, Ohrlänge und „Curling“ der Zunge, führendes Auge und Haarform, führendes Auge und Haarwirbel, Augenfarbe und Fingerbehaarung.

3. 7 Koppelungen mit einem für Koppelung wahrscheinlichen χ^2-Wert: Fingerlänge und Haarwirbel, Fingerlänge und Händigkeit, Ohrlänge und Ohrläppchen, P.T.C. und Ohrläppchen, P.T.C. und Haarform, Ohrläppchen und Händigkeit, Händigkeit und Haarfarbe.

Als neues Chromosomenmarkierungsmerkmal wurde das „führende Auge" eingeführt, für welches wir eine Koppelungsbeziehung mit Haarform und mit Haarwirbel wahrscheinlich machen konnten.

BIBLIOGRAPHIE

Bernstein, F.: Z. ind. Abstam. u. Vererbg.lehre *57*, 113, 1930. – *Bernstein, M.* et *B. S. Burks:* J. Hered. *33*, 45, 1942. – *Boyd, W. C.* et *L. J. Boyd:* Ann. of Eug. *8*, 46, 1937; *2*, 1, 1941. – *Burks, B.:* Yearb. of Carn. Inst. *36*, 312, 1937. – *Burks, B.* et *H. Wyandt:* Genetics *26*, 223, 1941. – *Chamberlain, H. B.:* J. Hered. *19*, 557, 1928. – *Falconer D. S.:* Ann. of Eug. *13*, 211, 1946. – *Finney, D. J.:* a) Ann. of Eug. *10*, 171, 1940 b) Ibid. *11*, 10, 1941 c) Ibid. *11*, 115, 1941. – *Fisher, R. A.:* a) Ann. of Eug. *6*, 187, 1935 b) Ibid. *6*, 339, 1935 c) Ibid. *7*, 17, 1936. – *Franceschetti, A.:* Arch. Suisses de Neur. et Psych. *63*, 219, 1949. – *Guyénot, E.:* Actes Soc. Helv. Sc. Nat. *1940*, p. 57. – *Haldane, J. S.:* a) Ann. of Eug. *6*, 26, 1935 b) Ibid. *7*, 28, 1936 c) Ibid. *13*, 122, 1946 d) Proc. Roy. Soc. B. *135*, 147, 1948. – *Halpern, S. L.:* J. of Hered. *30*, 504, 1939. – *Hogben. L. T.:* Proc. Roy. Soc. B. *114*, 340, 1934. – *Hogben, L.* et *R. Pollack:* J. of Gen. *31*, 353, 1935. – *Klœpfer, H. W.:* Ann, of Eug. *13*, 35, 1946. – *Munro, T. A., L. S. Penrose* et *G. L. Taylor:* Proc. of the 7. Inter. Cong. of Gen. Cambridge 1939. – *Neel, J. V.:* The Am. J. of Hum. Gen. *1*, 19, 1949. – *Penrose, L. S.:* a) Ann. of Eug. *6*, 133, 1935 b) Ibid. *8*, 233, 1938 c) Ibid. *13*, 25, 1946 d) The Lancet *250*, 949, 1946. – *Rife, D. C.* et *H. W. Klœpfer:* The Ohio J. of Sc. *43*, 182, 1943. – *Rife, D. C.:* Science *94*, 187, 1941. – *Rywlin, A.:* Act. Gen. et Stat. Med. *2*, fasc. 1, 1950. – *Snyder, L. H.:* a) Z. f. Imm. Forsch. *49*, 464, 1926 b) Proc. of the 8. Inter. Cong. of Gen. *1949*, 446. – *Snyder, L. H., R. C. Baxter* et *A. W. Knisely:* J. of Hered. *32*, 22, 1941. – *Snyder, L. H., H. Russell* et *E. B. Graham:* Science *106*, 347, 1947. – *Wiener A., S.:* Genetics *17*, 335, 1932. – *Zieve, I., A. S. Wiener* et *J. H. Fries:* Ann. of Eug. *7*, 163, 1936.

COMBINATIONS AND SEQUENCES OF SEXES IN HUMAN FAMILIES AND MAMMAL LITTERS

A Review of Literature with Comments and Some New Results

by CORRADO GINI

Many statistics and a whole literature exist on sex ratio in human births, but comparatively few data and few writings deal with the combinations and the dispositions or sequences of sexes in human families.

The questions that have attracted the attention of the researchers in this field may be grouped under the three following headings:

1. The conformity of the observed sex combinations or sequences to (or the divergency from) those which are to be expected as the effect of random variation;
2. The effect of the wish of parents to have a child of a certain sex;
3. The heredity of sex.

We shall examine the three points separately and close our report with some remarks on the combinations of sexes in mammal litters.

* * *

The first data on the subject seem to be those for the town of Middelburg (Holland) published in 1855 by *L. Janse* (1). They relate to 2,412 families with 8,118 children. The sequences of sexes in each family were given, but no comparison was made with a random distribution.

A much wider and more thorough research was made by *A. Geissler* (2), who in 1889 published data on the combinations of the sexes in the families, as they were given by the parents at the birth of each child, in the kingdom of Saxony from 1876 to 1885. The statistics referred to almost one million families (exactly 998,760) with almost 5 million children (exactly 4,794,304). *Geissler* submitted the data to several detailed elaborations and compared the results

with those that were to be expected in random distribution, that is, if the probability of a male birth were constant for all the families and for all the births in each family.

His conclusions were:

1. An excellent agreement exists between the observed frequency of the different combinations of sexes in the families and the frequency expected in random distribution.

2. A compensatory tendency generally exists between the sexes of the successive births, so that after many boys the probability of a female birth increases and, viceversa, after many female births the probability of a male birth becomes greater, except for the same-sexed families (with all males or all females) who—owing to some special factors—have a higher probability of having a child of the same sex as the previous ones.

The two conclusions—without any further addition—appear contradictory in as much as, should the second be true, the observed frequencies for the median combinations would not agree with, but would instead be higher than the calculated frequencies.

Geissler's data have been submitted to more refined elaborations in the first years of this century by *Corrado Gini*, who was also able to elaborate new data relating to 74,558 births that occurred during the years 1891–1901 in the families of the city of Dresden with two to six children. The results have been presented in *Gini*'s doctor's thesis submitted in 1905 to the University of Bologna and awarded the *Victor Emanuel* prize (3) and then in a book published in 1908 (4) and in an article that appeared in 1911 (5). Unfortunately, these works written as they were in Italian, were unknown until recently to most of the later authors.

In the meantime, two articles appeared: one in 1904 by *S. Newcomb* (6), based on data relating to 7,896 American families, partly (1812) extracted from the United States Census of 1900 and partly (6,084) from American genealogies; and the other in 1905 by *J. B. Nichols* (7), based on data extracted from the genealogies of New England, relating to three thousand families having at least 6 children. Both came to the conclusion that the observed frequencies of the sex combinations correspond exactly to the theoretical ones.

Later on we will discuss the apparent disagreement between their conclusions and those of *Gini* mentioned above.

For the sake of completeness another writing must be mentioned.

Orchansky, a Polish doctor, in 1894 presented to the Imperial Academy of Warsaw a treatise that the following year was translated into Italian by *C. Lombroso* (8). *Orchansky* thought he had demonstrated that some families have a tendency to produce male and others to produce female offspring and that the same couple, during certain periods, has a tendency—due to the general condition of the wife—to produce one sex, and during certain others, the other sex. But both his conclusions lacked any statistical foundation. The first was based on the fact that in the families whose first child was a male, the male sex prevailed and, on the contrary, in those whose first child was a female, the female sex prevailed; but this was only the effect of the sex of the first birth. If the first birth is excluded—as it should be—the difference disappears. The second conclusion was based on the fact that all the children of a family rarely are of the same sex; but it is evident that this may depend on random variation and does not prove that a modification occurred in the tendency to produce one or the other sex.

Gini's extensive researches (1905, 1908, 1911), partly made by new statistical methods, allowed the author to elucidate this question, eliminating the apparent contradiction of *Geissler*'s conclusions.

Using *Geissler*'s data he showed indeed that there is a tendency in the families to produce either one or the other sex, a tendency which however seems general and not limited to the same-sexed families only. But the data also showed that this tendency may change in the course of time so that in the families who first had a propensity to produce males, this propensity progressively declines possibly giving place ultimately to the contrary propensity to produce females, and, vice versa, in the families who first showed a propensity to generate females, this propensity decreases gradually, changing over eventually to a propensity for males. These conclusions were formulated already in *Gini*'s doctor's thesis (9), in which moreover the author drew the curves of the variations of such a tendency as the resultants of the hypothetical individual curves of the influence of husband and wife in determining the sex of the child (9 bis).

In the following book on *Sex from a Statistical Point of View* (1908), *Gini*, extending to individual families the dispersion coefficients, introduced a rigorous method for measuring the family tendency to produce one sex, and applied it, together with other methods, to *Geissler*'s data for Saxony, to his new data for Dresden and to other data extracted from the literature. He came to the

conclusion that about 10–15 % of the observed family differences in the combination of sexes represent the systematic component due to such tendencies, while the residual 85–90 % represent the accidental component due to random variation that would vanish, if the families had a very great number of children (10).

Another method—based on a new scheme of a posteriori probability—was introduced by *Gini* in 1911 making it possible to separate the effect of the family tendency to produce one sex from that of the systematic variations of such a tendency. He could thus follow the progression of such a variation during the marriage and measure its intensity according to the combinations of the earlier births (11).

At this point substantial progress in the matter could be expected only from more detailed statistics, furnishing not only the combinations but also the dispositions or sequences of the sexes in the individual families.

Such researches were undertaken in 1912 at the University of Cagliari, under the direction of *Gini*, by *G. Asquer* for the families of the Italian nobility (12). They referred to the births in the families of the different regions of Italy listed in the beginning of the 20th century in the register of the Italian nobility, and particularly the births in the families of the nobility of Cagliari during three centuries (1599–1897) as shown by the data extracted from the parish registers.

For families with less than 6 children a direct comparison was made between the observed sex sequences and the theoretical ones which might be expected in the case of random distribution, with the result that, not only for the same-sexed families, but also for the families in which the children of one sex are followed by children of the other sex, the observed frequency exceeds the theoretical one, while the families in which the succession of the sexes is irregular are less frequent in reality than in theory. This result confirms the tendency of individual marriages to produce one sex as well as its inversion during the procreation. This inversion recalls the well-known fact that in many bisexual species the two sexes are functioning alternatively, either first the male and then the female sex, or first the female and then the male one. Thus the inversion of the propensity to procreate one sex may perhaps be considered as a residual of such an alternation which occurs in the bisexual stage of evolution.

For families with six or more children, the research has been limited to the counting of permanences or variations of the sexes in

two successive births, it being understood that there is a permanence when a male is followed by another male or a female by another female, and a variation when a male is followed by a female or a female by a male. The observed number of permanences is slightly superior (and consequently that of variations slightly inferior) to the calculated one in case of independence, which is in agreement with the abovementioned results.

One of the main purposes of future researches should be to control the results above described.

Doctor *A. Prevosti* of the Anthropological Laboratory of Barcelona, working in 1948 at the Institute of Statistics of the University of Rome under the direction of *Gini*, on material collected by *Gini* in past years, elaborated data concerning families of soldiers who died during the First World War, families of Roman Civil Servants, sovereign, mediatized and noble families of Europe extracted from the Gotha Almanach as well as the noble families already considered by *Asquer*, families of psychopathic patients, and a group of Venetian families observed by *Gini* himself. The results obtained confirm the conclusions reached by *Gini* on *Geissler*'s data, but they also show some irregularities, due perhaps to the smallness of some series, but to which in any case further attention must be given.

The results obtained by *Gini* and *Asquer* on the Italian nobility, showing an excess of the same-sexed and one-sex-variation families, have been confirmed by the elaboration, made also under *Gini*'s direction at the Institute of Statistics of the University of Rome, of the abovementioned data of Middelburg published by *Janse*, as well as of other data concerning a group of large (with 7 or more children) Italian families.

The progressive variation and possibly the inversion of the tendency to procreate one sex gives paramount importance to the following distinctions:

a) between complete (a_1) and incomplete (a_2) families, that is, between families whose procreation has finished or else is still in course. The data extracted from the censuses include many incomplete families, while those extracted from genealogies usually concern complete families;

b) between data collected at every birth (b_1) and data collected only once for each family (b_2). *Geissler*'s data are of the former description, those extracted from genealogies or censuses of the latter.

When the sequence of sexes is given it is possible to pass from the data b_1 to data b_2 and vice versa;

c) between complete families in which the procreation was exhausted (c_1) and those in which it was not (c_2). The marriages which have been interrupted by divorce or death before husband or wife had passed the procreation limit are of the second kind, as well as those in which the procreation has been interrupted by an infirmity of one of the partners or by voluntary interruption of procreation;

d) between marriages which had been contracted when both the partners were very young (d_1), so that they may be considered to describe their whole reproduction cycle and those in which one or both of the partners were already advanced in age (d_2);

e) between the families of the category (c_2) who interrupt their procreation without giving any consideration to the sex of the preceding children (e_1) and those who at the said interruption pay attention to the said circumstance (e_2). In the category e_1 substantial modifications in the combination of sexes may occur as the effect of the preference for one or the other sex, so that we will treat this subject in a special paragraph.

It is evident that in order to obtain a complete picture of the tendency for married couples to have children of one or the other sex, as well as of the variation that this tendency presents, it would be necessary to consider marriages contracted at a very young age and lasting till the closing of the procreation period, and moreover, not practising any birth limitation nor being interrupted in their normal reproduction activity by infirmities or prolonged absences of one partner. This may have been the case in past periods with the marriages of the peasant population or of sovereign families.

In the abovementioned researches, Dr. *Prevosti*, having at his disposal many series of data for which the sequences of sexes were known, could compare the theoretical and observed sex combinations for data b_1 with those of data b_2. The data b_2 conform to the theoretical frequencies better than data b_1, as was to be expected owing to the change of the tendency to produce one sex.

Not less important is the result, also obtained at the Institute of Statistics in Rome, by comparing *Geissler*'s data for Saxony as well as *Gini*'s data for Dresden, which are of category b_1, with the respective data a_1 which can be deduced from the same statistics. While data b_1 show, as has been said, a variability distinctly superior

to the theoretical one, the variability of data a_1 conform to the theoretical expectation. This may explain the disagreement between the results obtained in the past by *Nichols* and *Newcomb* on data completely or for the most part extracted from genealogies and those obtained by *Gini* and other authors on *Geissler*'s data and other data for incompleted families.

Another suggestive finding of the researches in course at the Institute of Statistics of the University of Rome concerns the different frequency with which the marriages continue procreation according to the different combinations of sexes among the children already born. On *Geissler*'s data it is possible to establish that, not only marriages which so far had only males or only females, more frequently have a further child—as might be expected if they desire either a boy or a girl—but that, among the other marriages, the frequency with which procreation is continued is generally lower when the distribution of the sexes in the earlier children is better balanced, falling to a minimum when the maximum equilibrium is attained. This fact is all the more remarkable as, at the time of *Geissler*'s statistics (around 1880) birth control was presumably little practised in Germany. It suggests indeed that sex equilibrium often marks the end of the procreation period.

This result may possibly be connected with another quite unexpected and so far unexplained one, reached 20 years ago by *Gini* and his collaborators in an investigation into large Italian families (with 7 or more children) (14). It was then shown that the sibships of the fathers of such families (the propositi obviously excluded) had an unusually high proportion of males; on the contrary, the sibships of their wives, that is of the mothers of the large families, had (also excluding the propositae) an unusually high proportion of females.

* * *

We shall now pass to review the results obtained by several authors since *Gini*'s researches and mainly independently of them.

The reliability of *Geissler*'s data has often been discussed.

Geissler himself had put the question whether the inclusion of multiple births, which are often of the same sex, could contribute sensibly to the excess in the frequency of the same-sexed families. The unanimous reply of all the authors who paid attention to this question has been, however, negative. (Cf. *R. A. Fisher* [15], *G. H. M. Waaler* [16], *R. J. Myers* [17], *C. Stern* [18]).

Another supposition was advanced by *R. A. Fisher* (1925). Examining the sex combinations in families of 8 children, he remarked that there is an apparent bias in favour of even values for which no biological reason is suggested, so that he thought that the discrepancy depreciates the value of the data (15). From the diagrams constructed by *Gini* (19), analogous slight biases in favour of even values may be observed in *Geissler*'s data for the families of 4, 6 and 12 children (not for those of 2 and 10 children), as well as for the families of 5, 7 and 9 children (not for those of 3 and 11 children) and similarly in *Gini*'s data for Dresden for the families of 6 children (not for those of 2, 3, 4 and 5 children). At the present state of our knowledge of sex determination—though very limited—it is difficult, however, to assert that they allow no biological explanation. In his doctor's thesis (1905), *Gini*, having duly noted them, explained them as the result of the inversion of the family tendency to produce one sex (20). *Slater* suggests that it may be the effect of the compensation of the tendency of the father to produce one sex and of the mother to produce the other sex (21).

Quite recently a special article has been written by *H. O. Lancaster* (22) for the purpose of demonstrating that *Geissler*'s data are biased, probably because of careless answers by parents. The bias towards even numbers—he remarks—is notorious in demographic data; so the parents may have sometimes erroneously declared an even number of males and females among the total children.

Lancaster thinks that the bias is confirmed by the fact that the same tendency does not appear from the data for the children preceding the last.

It seems, however, that *Lancaster* did not pay attention to the fact that—as is clear from *Geissler*'s article (23)—the question addressed to the parents was not: How many males and how many females have you? but in the first place: What is the number of children from this marriage you have reached with the declared birth? And then, according to whether the last-born was a boy or a girl: What is the number of boys (or of girls) you have reached with this birth? Now it is much less probable that a bias may prevail in replies to questions thus formulated.

The absence of the prevalence of even combinations among the children preceding the last, may be explained by the abovementioned fact that families in which the two sexes balance continue procreation less frequently.

Other curious anomalies and inconsistencies that *Lancaster* thinks he has observed in *Geissler*'s data and that in his opinion cannot be due to any biological mechanism do not really exist. If *Lancaster* had known the literature on the subject better, he would have found that the supposed inconsistencies were discussed in it and explained. This is particularly the case for the significantly low probability of a male birth in families which had but one female with an excess of males.

To sum up, it is difficult to see any serious reason for doubting the reliability of *Geissler*'s data, all the more so as the general accuracy of German statistics is well recognized. In any case, to throw doubts on the accuracy of figures which you cannot explain is a very risky proceeding, only admissible in the case of scholars who have studied the subject thoroughly.

* * *

Admitting the reliability of *Geissler*'s data, several explanations of the systematic discrepancies between observed and theoretical frequencies of the sex combinations have been tried (1928) by *Waaler* (16).

An explanation based upon the higher ratio of males in abortions and upon the presence of lethal factors linked to sex proved insufficient. He found, however, that the discrepancies could be explained by the hypothesis that different women have a different tendency to produce males and that this tendency varies systematically in the same woman from one birth to another, leading to a compensation between the past sex combinations and the sex of the new-born, except in the case of same-sexed families which tend to produce prevalently the same sex. With this exception, that *Gini* had already proved to be inexistent, *Waaler*'s conclusions seem to be the same as those reached by *Gini* in his writings of 1905, 1908 and 1912 with which *Waaler* evidently was not acquainted.

Waaler's article being written in Norwegian with a short German summary, it is difficult for those not conversant with the Norwegian language to grasp its details, which are, on the other hand, essential for judging the foundation of his demonstration. It seems, however, that it involves hypotheses which, on the one hand, are debatable and, on the other, are unnecessary. As a matter of fact no hypothesis had been made by *Gini* when, many years before, he had reached the same conclusions.

Waaler has also remarked that, according to *Geissler*'s material, the families which have a new child are selected from those with more males; a more correct description of the fact is, however, as we have said above, that the said families are selected among those in which either the one or the other sex is prevalent.

Lastly, *Waaler* pointed out that this selection, as well as the variation of the tendency of the individual woman to produce one sex, have no biological explanation, while an explanation of both is possible and has already been mentioned.

It is necessary to arrive at 1937 in order to find another article on sex combinations in human families. It is an article by *Rife* and *Snyder* (21) who collected and elaborated data on 1643 families, probably in the most part incomplete, living at Grandview Heights near Columbus (Ohio). Comparing their sex combinations with the theoretical ones in the random distribution hypothesis, they declared that there was a satisfactory agreement; but really the frequency of the extreme sex combinations is deficient for the families with 2, 3 or 4 children, while irregularities, evidently due to the small number of observations, prevail for the families with 5 children.

The article by *Rife* and *Snyder* was the only one based on facts quoted by *Myers* (17) in an article published in 1949 in which he examined the data of 999 families (most of them probably incomplete), extracted from the American Who's Who ? The discrepancies between the observed data and the expected ones on the random distribution hypothesis are considered as not significant, except for the two-children families for which the observed deficit of same-sexed families is attributed to the wish to have a further child of the opposite sex.

It is to be mentioned that *Myers* speaking of a possible excess of the same-sexed families thinks it obvious that it be caused by a special mechanism limited to these families and not—as *Gini* has already proved—by a general tendency of the parents to have one sex, the excess of the same-sexed families being only a particular manifestation of such a tendency.

Some years before a special research had been made by *Slater* (21) on a psychopathic population composed of 1,007 patients (909 males and 98 females) admitted to Sutton Emergency Hospital during the years 1939–41. *Slater* rightly omitted the twins and the propositi (this is justified in as much as his propositi were mainly males). He also omitted individuals of unknown sex instead of omitting the whole sibships in which these individuals occurred. On the other hand he

considered, besides the sibs of propositi, their children and the children of each sib, obtaining data for 1,228 families with two or more children showing a slight excess of females (3.638 males and 3,762 females). The mean age of the propositi (28,3 years) suggests that their families, as well as the families of the other sibs, are generally incomplete, while their sibships may be considered as complete.

Slater found an excess of the observed over the theoretical number for the same-sexed families as well as for the families with a strong preponderance of one sex, a slight deficit for the families with absolute equality of the two sexes and a more marked deficit for those with a more marked excess of one sex. These results are quite in keeping with those obtained on *Geissler*'s data.

Another elaboration suggested to *Slater* by *R. A. Fisher* has been to count the frequencies of all the possible relations brother-brother, sister-brother, brother-sister and sister-sister, between the members of the same family, with the result that the relations brother-brother and sister-sister are significantly more numerous than those brother-sister and sister-brother—a result which confirms the tendency of individual families to produce one sex.

At the 1948 International Congress of Genetics at Stockholm, *Turpin* reported on some researches made by him and *Schützenberg* on 14,230 French large families (from 5 to 19 children, the families with multiple births being omitted) (25), whose results were published with more details in an article which appeared the following year in the "Semaine des Hôpitaux" (26). In spite of the fact that at the Congress of Stockholm *Gini* called the attention of the authors to the substantial agreement between their results and those attained by him many years before, *Gini*'s works have not been cited in their article of 1949, nor has a note sent by *Gini* some months ago to the "Semaine des Hôpitaux" so far been published (26).

As a matter of fact the authors also have found, like *Gini*, a variability of the sex combinations higher than the theoretical one, a slightly positive correlation between the sexes of the successive births and, for the same sex combinations, a higher frequency of the sequences in which the number of variations is lower. Like *Gini* they have properly had recourse to the examination of sequences in order to separate the influence of the variations of the probability of producing one sex during the procreative life of the marriage from the influence of the tendency of the family to produce one sex.

They differ, however, from *Gini* when they think that the higher frequency of the sequences with fewer variations may be explained either by a frequency change of the tendency to produce one sex by the same marriage or by the influence of the sex of a new-born on the sex of the following one.

Now, the second hypothesis may be considered excluded by the mechanism of sex determination in a male heterogametic species like the human.

As to the first hypothesis, it is difficult to agree with the statement of the authors in the article of 1949, according to which the periods favourable to the birth of males and those favourable to the birth of females are distributed at random over the procreation period and without being connected with its beginning nor with its end. *Gini*, on the contrary arrived at the conclusion that generally the marriage begins with the tendency to procreate one sex and ends with the tendency to procreate the opposite one. This inversion of the tendency to procreate one sex is proved by the fact that the frequency of the sequences with only one variation is in the material examined by *Gini* higher and the frequency of the sequences with two variations, on the contrary, is lower than the theoretical ones. This result seems to exclude the abovementioned hypothesis of *Turpin* and *Schützenberg*.

The authors also wrote that some elaborations which they had made suggested that the interval between two successive births of the same sex is generally shorter than that between two successive births of different sex, a result which they think supports their conclusion but which is really equally in keeping with the conclusion of an inversion of the tendency to procreate one sex.

One full chapter is dedicated to the sex ratio in the recent treatise on *Human Genetics* by *Stern* (18), some pages of which speak especially of the combinations of the sexes in human sibships. The literature referred to is almost exclusively American—only *Geissler* being cited among the Europeans who have contributed by original researches to the study of sex combinations. The author seems to adhere to the idea that the excess of same-sexed families depends on a special mechanism acting in some of them, rather than on a general tendency of the marriages to procreate one sex.

* * *

The wish to have a child of one rather than of the other sex and birth control furnish a characteristic example of two agents whose cumulative effect is quite different from the sum of their separate effects.

We are speaking of their effect on sex combinations of families. Without birth control the wish to have a boy or a girl has most probably no influence at all on the sex of the new-born in spite of the contrary idea advanced in the past by some wellknown statisticians like *v. Oettingen* (27) and *v. Mayr* (28).

Without the wish to have a child of one sex, birth control has probably some effect on the combination of sexes. As a matter of fact, if in each family there is a tendency to have one sex which is progressively changing until it gives place in many cases to the opposite tendency, it is to be expected that birth control practices, in as much as they limit the procreation to the first phase of the sexual cycle, accentuate the uneven combination of sexes. It may be that a difference between the results obtained by *Gini* on *Geissler*'s data for Saxony and those obtained on his own Dresden material depends precisely on this circumstance. As a matter of fact birth control around 1880 was probably of very limited importance for the general population of Saxony, while in the first decade of our century it had certainly assumed remarkable importance for the urban population of Dresden. Now the systematic component of the variability of the family sex combinations is higher for Dresden (13 %) than for Saxony (11 %) in spite of the fact that the contrary was to be expected, as the variability for Saxony referred to families of 2 to 12 children, while those for Dresden only to families of 2 to 6 children and, obviously, the accidental component is lower and the systematic one higher the greater the size of the family.

Different—even opposite—may be the effect of birth control if it acts through postponing the first pregnancy and/or spacing the successive ones.

For a similar reason, also the age at the marriage, having the effect of initiating the procreation at a phase more or less advanced of the sexual cycle and consequently influencing the evolution of the tendency to procreate one sex, may have some effect on the sex combinations of families.

But it is when birth control is associated with the wish to have a child of one sex that its effects on the sex combinations of families become important.

Its effects are not substantially different if they act through stimulating procreation when the desired sex is still lacking—as occurred especially formerly—or through stopping procreation once the desired sex composition is obtained—which occurs especially in the present times.

They are obviously different when both the parents desire a boy or a girl or, on the contrary, when one parent wishes a boy and the other a girl. And the wishes of the parents may be different in the various social classes (for example, in the nobility and in the bourgeoisie) and may depend on the different sex combinations of the earlier living children.

On this important point everybody has his own impressions; some writers have also made inquiries among their acquaintances (for example, *Sanford Winston* [29]), but the only systematic research—so far as I know—has been made by *G. Dahlberg* (30) in Sweden, on 907 marriages of patients recorded in the Academic Hospital of Uppsala and in the General Hospital of Malmö before the child was born.

The replies of the couples who had no child do not directly interest our present discussion; among the others, the marriages which had only or mainly boys preferred a girl to a boy in an overwhelming number of cases (86 %) and even more frequently (in 90 % of the cases) a boy was preferred to a girl when the marriages had only or mostly girls, the sex being indifferent only in somewhat more than 10 % of the cases. When, on the contrary, the marriages had an equal number of boys and girls, the parents were very often (in 44 % of the cases) indifferent to the sex of the new-born, and, if they were not indifferent, they divided their preferences, both wanting almost equally often a girl as a boy, or, on the contrary, the father wanting a boy and the mother a girl. These data do not only show the desire of the parents of having both the sexes represented among their children, but also reflect the stronger desire for boys and some preference of each parent for a child of his own sex.

Among the total of 1,814 replies obtained from all the parents interviewed, about 39 % wanted boys, 33 % girls and 28 % were indifferent. It is obvious that during other times and in other countries the wishes may be different, and so it is very probable that the preference for boys was much stronger in older times and is, in recent times also, much stronger in those countries where the economic and social advantage for the family of having a boy is higher.

Dahlberg's inquiry, in which also the sex of the new-born was asked, confirmed its independence of the wishes of the parents.

What the effect is of the divergent wishes of the parents, when birth control is practised, may be for the present a matter of speculation and for the future a matter of new inquiries, but it is obvious that the common wish of the parents to have a child of one sex induces them, if the wanted sex is still lacking, to continue the procreation that otherwise would be arrested, and, on the contrary, as soon as a child of the desired sex is born, to stop the procreation that otherwise would be continued.

In times when the preference for boys appeared general, it was consequently thought that the parents arrested or did not push procreation when they had obtained a boy, and the theory had been advanced that this circumstance must enhance the proportion of boys and might even explain the excess of male births in human populations.

In this consists the so-called "psychological theory" of the excess of males in human births presented in 1829 by *Prévost* (31) and accepted by no small numbers (32). Even in our times it is implicitly admitted by some authors, for example by *F. A. Woods* (33), who expects that the wish to have boys in sovereign and princely families should determine a higher proportion of males in their children. The error of such an expectancy has been pointed out to *Woods* by *Norton* (34) and, in a general form, it is noted by several authors, for example by *Stern* (35). It had already been fully put in evidence in *Gini*'s doctor's thesis (36) and noted also in his book (37).

On the other hand the affirmation by *Norton* that the desire to have a boy cannot influence the sex ratio of the births just as the desire to gain does not influence the result of a game of chance, is also inexact. It would be true, if the sex combinations followed exactly the random distribution; but, as we know, this is not the case. Different families have a different tendency to produce males and females: those who have a tendency to produce females are more likely not to have produced males in the previous births and to be induced consequently to continue procreation in order to have a boy. It is then to be expected that the wish to have a boy, inducing procreation in families with a tendency to have females, disturbs the sex ratio of the births, but not in the sense suggested by *Prévost* through increasing the proportion of boys but rather in the opposite sense by increasing, though slightly, the proportion of females. This effect

was duly put in evidence by *Gini* (38) who had also suggested that the endeavour to have a boy in the unisexual female families being more intense than the endeavour to have a girl in the unisexual male families, might explain the markedly higher excess over the theoretical frequency of the observed frequency of the unisexual female families in comparison with the observed frequency of the unisexual male families—a difference that he had clearly shown on *Geissler*'s data for Saxony as well as on his own data for Dresden (39). In the same work, *Gini* had also presented data suggesting that, in Dresden as well as in Saxony, the unisexual female families continue procreation more often than the unisexual male families (40).

So far we have considered data of type b_1, in which (as was the case with *Geissler*'s statistics for Saxony and with *Gini*'s for Dresden) the sex combinations are observed at every birth. For such data the only effect of the wish of parents to have a male or a female after a same-sexed combination in the preceding children is to enhance in the families with a higher number of children the uneven sex combinations which ensue from marriages in which reproduction is continued because of a missing sex. But, when we consider data—concerning families complete or incomplete—of the type b_2, such as those extracted from censuses or genealogies, the alteration consists not only in exaggerating the frequency of the uneven sex combinations in the families with more children, but also in diminishing the frequency of the same-sexed families with few children.

Moreover, no influence of the wish to have boys on the sex ratio of the last children of the family is to be expected in data of type b_1, while it is to be expected that in data of type b_2, relating to complete families, a higher proportion of males occurs than among the preceding births.

The numerous authors who in recent times have treated the question and whose researches we have reviewed, have failed to pay attention to these important differences to be expected between data of type b_1 and of type b_2.

Comparisons of the sex ratio among last children with that among previous children or among all the children of the families, have been published in 1939 by *Woods* (33) for the sovereign houses and mediatized princes according to the data of the Almanach of Gotha of 1923. They were criticized, in the following year, by *Norton* (34), but, on the whole, one cannot deny that, in the data presented, the sex ratio is higher among the last children than among their

preceding sibs. It should be remarked that the families of the Gotha Almanach were not necessarily complete, so that the material was not the best suited for showing the influence of the preference for boys.

Clearer was the influence that some years before (1932) *Sanford Winston* (29) had found when examining the data, extracted from the Abridged Compendium of American Genealogies, for 5,465 families of an economic and social standing superior to the median, which could be considered complete.

Similar researches, but on a very much greater scale, had been made in 1912, under *Gini*'s direction, by *Asquer* (12). They refer to the noble families of Cagliari during three centuries (1599–1897), as shown by the data of the parish registers, to the families of the nobility of the different regions of Italy, to the sovereign, mediatized and other princely families listed in the Almanach of Gotha of 1911 and to a group of civil servants of the city of Rome. For the families of Rome, as well as for those extracted from the Almanach of Gotha, only those have been considered which had completed the procreation cycle, while those of the nobility of Cagliari, relating to past centuries, were obviously complete. The observed number of males among the last children has been compared with the number which was to have been expected after allowing for the different sizes of families. The result was that, in all the groups of families, the observed number of males was inferior to the expected one, except in the case of the Rome families, for which it was slightly (5 %) superior. It is then evident that—except perhaps among the Roman civil servants—there was no control of births connected with the sex of the children. As for the sovereign or mediatized families, these conclusions must not be necessarily considered as incompatible with the results obtained by *Woods*, but can plausibly be interpreted as reflecting for 1911 a condition which was different from that of the date (1923) to which *Woods*' data referred.

An influence upon the sex combinations of sibships of the desire of the unisexual families to have a child of the missing sex could be inferred—but was not inferred by the authors—from the abovementioned data of *Rife* and *Snyder* (24). Its influence was asserted, as we have said, by *Myers* (17) on his own data, as well as by *Stern* on the basis of a research on a British population whose author and details he does not mention (41). In 1950, Miss *Marianne E. Bernstein*, who had already in 1948 treated some questions related to the sex ratio in human births (42), presented to the Seminary of the Institute of

Statistics of the University of Rome an interesting paper in which, by means of a simplified theoretical scheme, she has shown the influence on the sex combinations of sibships of the higher frequency of continuing procreation in the same-sexed families. Applying her scheme to 2,964 complete families listed in the American Who's Who, she has shown that the results obtained by *Rife* and *Snyder* and *Myers* could not be considered in contrast with the tendency of families to procreate one sex which on *Geissler*'s data had already been asserted by *Gini* and *Waaler* (43).

* * *

An alternative method for deciding if there are or are not differential tendencies in the production of one sex in different families, is to study the genealogies in order to ascertain if the sex combinations are inherited.

As a matter of fact only what exists can be inherited, so that inheritance of sex combinations has to be considered as a definite proof of the existence of a family tendency to produce one sex. On the other hand, as the physiological characteristics generally depend in some degree on genetic factors, it is to be expected that, should a family tendency exist, it would be inherited in some measure.

Special researches published in 1906 by *Woods* (44) on man and by *Heron* (45) on man and horse had led the authors to conclude that there is no heredity of sex. *Gini*, however (46), put the finger on the weak point of their demonstrations which is that they did not eliminate the effect of chance on the sex combinations of parents and children sibships that they correlated. *Gini* also gave the exact formula to be used in that case for the correlation coefficient, and applied it to *Wood's* and *Heron*'s data, coming to the conclusion that sex is inherited in substantially the same measure as other characters. To the heredity of sex, *Gini* dedicated a full chapter in his above cited book, making considerations that, in spite of the long time passed, may be substantially confirmed; he concluded that, in the determination of sex, both parents must directly or indirectly, contribute (47).

Since then, not many systematical researches on sex heredity in general populations have been made, but in any case several results and observations confirm the affirmative answer given by *Gini*.

It has been shown (*King*, 1919) to be possible to produce high and low sex ratio strains by continued selection within an animal stock, a result which implies that the tendency to produce more males or females than usual is inherited (48).

Examples of human families in which the excess of one sex is present in successive generations are often mentioned (cf. *Stern* 1949 [49], *Turpin* and *Schützenberg* [26]) but—leaving aside the uncertainties of genealogies in which the less interesting cases may be omitted—these observations do not by themselves prove the inheritance of sex more than the existence of same-sexed families proves the tendency to procreate males or females. To consider genetic factors established, it would be necessary to prove that the prevalence of the same sex in the families of successive generations is more frequent than would be determined by chance. On the other hand, it is quite possible that in some families special abnormal mechanisms intervene, analogous to those that have exceptionally been observed in some animal species (50).

A suggestion of the inheritance of sex is given by a result obtained by *Slater* (21) who, having added to the sibs of the propositus his children and the children of his sibs, obtained families in a wider sense which showed in their sex composition differences not less systematic than those observed in the families in the stricter sense. As a matter of fact this result suggests that the children of the propositus and of his sibs present differences in the same sense as those of the sibs of the propositus.

The subject has been attacked more directly by *Slater* who examined the sex preponderance in the children of the males pertaining to families with male preponderance and of the females pertaining to families with female preponderance. He found that they present in their children an excess of males or respectively of females over the number to be expected. Moreover, correlating the male and the female preponderance of one sex in parental generations with the preponderance in the filial generation, he obtained a positive association. Both results point to the heredity of sex-producing tendency.

On the other hand, it may be worth while to call attention to the fact that in *Slater*'s material the females of families with male preponderance do not present an excess of males among their children, nor do the males of families with a female preponderance present an excess of females among their children, a fact which may be considered

as confirming the conclusion that the presence of males in families with a prevalence of females as well as the presence of females in families with a prevalence of males does not depend only upon chance but is also the effect of a change occurring in the prevalent sex-producing tendency of the family.

* * *

The existence of a family tendency to produce one sex being demonstrated on a uniparous animal like man, it should be expected that something similar exists also in the pluriparous animals and that, consequently, the sex combinations of their litters show a variability higher than the theoretical one in the case of pure chance differences. Surprising as it may be, it is the contrary that often seems to occur, at least when the mothers live under the same conditions, as *Gini* (1908 [5]) and then *Boldrini* (1919 [51]) have shown for rabbits and mice and later *Parkes* (1923 [52]) confirmed for pigs. *Gini*'s and *Boldrini*'s data refer to laboratory experiments and are certainly accurate. Those of *Parkes* are extracted from the National Duroc Jersey Pig Report and the author does not deny the possible inaccuracies of the registrations, dependent both on the extermination of the least promising of a litter before the registration and on the omission of animals which die before registration, but he remarks that it is difficult to see how either of these inaccuracies could materially affect the frequency of the different sex combinations of the litters.

The abovementioned results obtained by *Gini*, *Boldrini* and *Parkes* are all the more remarkable as they furnish the unique examples so far known of a subnormal dispersion in statistical series.

Gini proposes the following explanation for species in which the male sex is heterogametic, as is the case for the mammals to which his researches and those of *Boldrini* and *Parkes* refer. Every male sexual cell gives origin, as is well known, to two male producing sperms and to two female producing sperms. Certainly the sperms deriving from the various sexual cells mix together when going towards the eggs but it is evidently not to be expected that, sampling a group of them, all the possible combinations of the two kinds of sperms will be in agreement with a random distribution, the extreme combinations in which one kind of sperm is totally absent being obviously less probable and those in which the two kinds are both

represented, especially those in which there is an even proportion of both, being more probable than according to the binomial theorem.

It is then to be expected that the eggs deriving from the same ovary, being fecundated by a group of sperms going one near the other, show the median sex combinations more frequently than would be expected by the calculus of probability, and consequently also the whole litter, derived from eggs produced by the two ovaries, may be expected to show a variability in the sex composition less pronounced than the theoretical one. It may be remarked that, according to the researches by *King*, a tendency to produce one sex exists at least in some animal species, and should this fact be considered as having a general character, we should expect, that, except for a possible compensatory mechanism, the sex composition of the litters would show a supernormal dispersion, so that the influence of the compensatory mechanism must be stronger than might be deduced from the difference between the theoretical and the observed variability. We will show later on that this inference is confirmed by some detailed data available for pig litters.

Other results, however, have been published in 1913 by *Wentworth* (53) for pigs and dogs and in 1915 by *Duncker* (54) for pigs, according to which the observed frequencies of the combinations would not present systematic divergencies from the theoretical ones.

The material of *Wentworth* is not presented in a form that allows of making elaborations similar to those made by *Gini*, *Boldrini* and *Parkes*.

The article by *Duncker* is important not so much for its conclusions as for the interpretation that may be given of its results and especially for the new researches that it suggests.

Duncker applies to the partial litters of pigs found in the same uterushorn and consequently produced by eggs coming from the same ovarium a method that he had adopted for determining the frequency of uniovular twins in human multiple births and finds that the observed combinations in the pig litters may generally be explained as the result of random variations without admitting that there are uniovular twins.

The method adopted by *Duncker* is, however, inacceptable in the case of human births, not only because it implies the hypothesis (as *Duncker* realizes) that none of the two-sexed combinations contain uniovular twins, but also because it implies the other hypothesis

(that *Duncker* seems not to realize) that there are no uniovular supertwins. In the case of human births both the hypotheses are certainly contrary to the truth.

As to pigs the existence of uniovular twins is suggested by the fact that sometimes pigs with double malformations are born which may be interpreted as coming from one egg. Now, it is to be remarked that the presence of uniovular twins and supertwins among the multiple births in same-sexed as well as in two-sexed families has the effect of increasing the variability, and that the larger the litter, the higher is the probability that two animals are uniovular twins. On the other hand, for the litters of two pigs, the observed frequencies of same-sexed combinations were according to *Duncker*'s data remarkably lower than the theoretical ones, thus being in keeping with the results obtained by *Gini*, *Boldrini* and *Parkes*.

The *Duncker* data could thus be interpreted in the sense that, independently of uniovular twins, there would be in the litters of two pigs a subnormal dispersion caused by a compensatory agent, but in the more numerous litters the influence of the uniovular twins or supertwins, increasing more than the number of animals, would have the effect of enhancing the dispersion, making it practically normal.

It is obvious that the frequency of uniovular twins or supertwins, as well as the tendency to produce one sex more than the other, may be different in the various multiparous species and even in the various races or stocks of the same species, so that it is not said that the groups of litters studied by the different authors must show the same degree of dispersion.

Duncker's elaborations were based on very detailed data concerning 1,000 litters of unborn but nearly mature pigs, available at one of the large slaughtering establishments in Cambridge, Mass., and published by *Parker* and *Bullard* (55).

The published records show for every litter the relative position of each pig in the uterus and its sex and allow of new elaborations. *Gini* has calculated the correlation between the sexes of two pigs in the same uterushorn, as well as between the sexes of two pigs in different uterushorns, finding that the correlation is in the first case very slightly negative and in the second slightly positive. The positive correlation between the sexes of pigs in different uterushorns may be attributed to a tendency of the sows to produce prevalently male or prevalently female pigs; while the negative correlation between the

sexes of pigs of the same uterushorn shows the effect of the compensatory mechanism explained above between the frequencies of the male producing and female producing sperms, which exceeds the contrary effect of the said tendency.

C. Gini [1]
Uppsala, Statens Rasbiologiska Institut
1st August, 1950

Summary.

The paper gives a survey of the results of researches published in different countries regarding the combinations and the dispositions or sequences of sexes in human families and in some mammal litters (mice, rabbits, pigs, dogs). The results of some researches in course at the Institute of Statistics of the University in Rome are also mentioned.

Résumé.

L'A. passe en revue les résultats des recherches publiées dans les différents pays concernant les combinaisons et les dispositions des sexes dans les familles humaines et dans les couvées de quelques mammifères (souris, lapins, porcs, chiens.)

Les résultats de quelques recherches en cours dans l'Institut de Statistique de l'Université de Rome sont également mentionnés.

Zusammenfassung.

In der Arbeit wird eine Übersicht gegeben von in verschiedenen Ländern publizierten statistischen Arbeiten über die Verteilung der Geschlechter bei der Geburt in menschlichen Familien und in Würfen von einigen Säugetieren (Mäuse, Kaninchen, Schweine, Hunde). Die Resultate von einigen Untersuchungen an dem statistischen Institut der Universität in Rom werden auch gegeben.

[1] This report has been written during a visit paid to the Rasbiologiska Institutet of the University of Uppsala, directed by Professor *G. Dahlberg*. I am greatly indebted to Professor *Dahlberg* for suggesting to me and putting at my disposal from the excellent library of the Institute several publications related to my researches and for his kindness in explaining to me some papers written in Scandinavian languages as well as for fruitful discussions on topics of common interest.

NOTES

1. *Janse, L.:* Bijdrage tot het onderzoek noar de Oorzaken der Geslachsverhouding bij de Geborten. Middelburg, Abrahams, 1853. – 2. *Geißler, A.:* Beiträge zur Frage des Geschlechtsverhältnisses der Geborenen. Das Geschlechtsverhältnis bei den Kindern gleichen Stammes. Zeitschr. des k. sächs. stat. Bureaus, XXXV. Jahrg., 1889. Nachtrag zu dem Artikel: Das Geschlechtsverhältnis bei den Kindern gleichen Stammes. Ibidem. – 3. *Gini, C.:* Intorno alla distribuzione dei sessi nelle nascite umane. Doctor's thesis presented to the University of Bologne (Victor Emanuel Prize), 1905. – 4. *Id.:* Il sesso dal punto di vista statistico. Sandron, Palermo, 1908 (actually for sale in the Library of "Metron", Institute of Statistics, the University Rome.). – 5. *Id.:* Considerazioni sulle probabilità a posteriori e applicazioni al rapporto dei sessi nelle nascite umane. "Studi economico-giuridici della Università di Cagliari", Ann. III, 1911. Republished in "Metron", vol. XV, 1949. – 6. *Newcomb, S.:* A Statistical Inquiry into the probability of Causes of the Production of Sex in Human Offspring. Carnegie Institution, Washington, June 1904. – 7. *Nichols, J. B.:* The Sex-Composition of Human Families. American Anthropologist, vol. 7, N. I; Jan.–March 1905. – 8. *Orchansky, I.:* Mem. of the Imperial Academy of Warsaw, 1894, June. Italian edition, with a foreword by *C. Lombroso*, with the title: L'eredità nelle famiglie malate. Bocca, Torino, 1895. – 9. *Intorno alla distribuzione* etc., pp. 122–125 and pp. 258–259. – 9 bis. Ibidem, pp. 128–131. – 10. *Il sesso etc.*, pp. 382–385. – 11. *Considerazioni etc.* See particularly "Metron" 1949, page 162 and tables I-VIII. – 12. *Asquer, G.:* Di alcune caratteristiche che il rapporto dei sessi offre nelle famiglie nobili italiane. Research worked out at the University of Cagliari (1912) under the direction of Professor C. Gini. – 13. *Prevosti, A.:* Estudio de algunos aspectos de la proporcion de los sexos en el hombre. Recently published by Instituto Bernardino Sahagun de Antropologia y Etnologia, Consejo Superior de Investigaciones Cientificas, Barcelona, 1950. – 14. *Gini, C.:* Opening speech by professor C. Gini, President of the International Congress for Population Studies (Rome 7–10 September, 1931), "Proceedings" Vol. I, Rome, 1933. – 15. *Fisher, R.A.:* Statistical Methods for Research Workers. pp. 69–71. Oliver & Boyd, London, 1925. 16. *Waaler, Georg H.:* Om seksualproportionen ved fodselen. Nord. Stat. Tidskr., pp. 65–84, 1928. – 17. *Meyers, R. J.:* Same-sexed families. J. of Heredity, Vol. 40, pp. 268–270, 1949. – 18. *Stern, Curt:* Principles of Human Genetics. Freeman and Co,. San Francisco, California, 1949. – 19. *Intorno alla distribuzione* etc., pp. 118–119, and *Il Sesso etc.*, diagrams at pages 380–382. – 20. *Intorno alla distribuzione etc.* pp. 120 and 131. – 21. *Slater, E.:* A Demographic Study of the Psychopathic Population. Annals of Eugenics, vol. 12, p. 2, 1944. – 22. *Lancaster, H. O.:* The Sex Ratios in sibships with special reference to Geissler's Data. Annals of Eugenics, vol. 10, p. 2. – 23. The questions made in the questionnaires from which Geissler's data are deduced are precisely: Das wievielte Kind aus dieser Ehe? und zwar: Der wievielte Sohn? Die wievielte Tochter? 24. *Rife, D. C.* and *Snyder, L. H.:* The Distribution of sex Ratios within Families in an Ohio City. Human Biology, vol. 9, pp. 99–103, 1937. – 25. *Turpin, R.* et *Schützenberger, M. P.:* Recherches statistiques sur la répartition des sexes à la naissance dans 14 000 familles d'au moins cinq enfants. Proc. of the Eighth Congress of Genetics. p. 678, Lund 1949. – 26. *Sur la distribution des sexes chez l'homme.* La Semaine des Hopitaux de Paris, La Semaine Médicale, N. 60, 25ième année, 14. 8. 1949. – 27. *Oettingen, A. v.:* Die Moralstatistik in ihrer Bedeutung für

eine Sozialethik. III. Auflage, Erlangen, Dreichert, 1882. – 28. *Mayr, G. v. e Salvioni, G. B.:* La statistica et la vita sociale, II edit. Torino, Loescher 1886, page 395. A Discussion of the so-called "theory of wish" of Oettingen and Mayr is made in *Intorno alla distribuzione*, pp. 151-54. – 29. *Birth Control and the Sex Ratio at Birth.* The American Journal of Sociology, vol. 38, n. 2, Sept. 1932. – 30. *Dahlberg, G.:* Do Parents Want Boys or Girls? Acta Genetica et Statistica Medica, Vol. I, pp. 163–167, 1948. – 31. The Theory was published in the "Bibliothèque Universelle de Genève". 1829, pp. 40 and ff. – 32. Between others from Boccardo, Levasseur, Mantegazza. For the bibliography on the subject see: *Intorno alla distribuzione etc.* p. 192. – 33. *The Inheritance of Strong Parental Instinct as Found in the Records of Royalty.* The J. of Heredity, vol. XXX, N. 6, June 1939 and N. 7, July 1939. – 34. *Norton, H. W.:* Note on Woods' Paper on Parental Instinct. The J. of Heredity, Vol. XXXI. N° I, Jan. 1940. – 35. *Principles etc.*, p. 391. – 36. *Intorno alla distribuzione etc.*, pp. 144–149. – 37. *Il sesso etc.*, page 167. – 38. *Intorno alla distribuzione etc.*, pp. 149–151.– 39. *Ibidem*, page 120. – 40. *Ibidem*, page 121. – 41. *Principles etc.*, page 391. – 42. *Bernstein, M. E.:* Recent Changes in the Secondary Sex Ratio of the Upper Social Strata. Human Biology, Vol. 20, pp. 182–194, 1948. – 43. The paper has been sent for publication to Human Biology. – 44. *Woods, F. A.:* The Non-Inheritance of Sex in Man. Biometrika, October 1906. – 45. *Heron, D.:* On the Inheritance of the Sex Ratio. Biometrika, October 1906. – 46. *Il sesso etc.* pp 396–398. – 47. *Il sesso etc.*, Chap. XI. *L'eredità del sesso*, pp. 394–434. – 48. *King, H. D.:* Studies in Inbreeding. Wistar Inst. Anat. and Biol., 1–175, Philadelphia, 1919. – 49. *Principles etc.*, pp. 396–397. – 50. See: *S. Gershenson:* A new Sex-Ratio Abnormality in Drosophila Obscura. Genetics, Vol. 13, pp. 488–507, 1928; *A. H. Sturtevant* and *Th. Dobzhansky:* Geographical Distribution and Cytology of Sex-Ratio in Drosophila Pseudoobscura and Related Species. Genetics, Vol. 21, pp 473–490, 1936; *F. A E Crew:* The Sex Ratio. Presidential Address, Section of Zoology of the Brit. Assoc. f. Adv. of Science, 1937. – 51. *Boldrini, M.:* Variabilità del rapporto dei sessi alla nascita nelle covate di alcuni mammiferi pluripari. Rendiconti della R. Accademia dei Lincei, Rome 1919. – 52. *Parkes, A. S.:* The Frequencies of Sex Combinations in Pig Litters. Biometrika, Vol. XV, 373 and ff., 1923. – 53. *Wentsworth, E. N.:* Sex in Multiple Births. Science, N. S., Vol. XXXIX. 24th April, 1914. – 54. *Duncker, G.:* Die Frequenzverteilung der Geschlechtskombinationen bei Mehrlingsgeburten des Menschen und des Schweines. Eine biostatistische Untersuchung. Biologisches Zentralblatt. Bd. XXXV, pp. 500–539, 1915. – 55. *Parker, G. H.* and *Bullard, C.:* On the size of litters and the number of nipples in swine. Proceeding Am. Ac. Arts Sc. Vol. 49 N°. 7 (Contr. Zool. Lab. of the Museum of Comp. Zool. Harvard Coll.. N°.239) pp. 399–426.

THE PRIMARY SEX RATIO AND ITS RATIO AT BIRTH

by GUNNAR DAHLBERG

The structure of society is basically determined to some extent by biological facts, although they permit of very great variation. The existence of about as many men as women is in reality a prerequisite for the monogamy which is found among most nations. If there were considerably more men than women, or vice versa, monogamy would not be feasible. Interest in the causes of the sex ratio at birth has for long been in evidence in view of the important bearing of the sex ratio on the structure of society.

We now know that considerably more male than female embryos are formed at fertilization and that abortions occur more frequently in the male than in the female. To some extent, the primary sex ratio is therefore evened out at birth, although a few more living boys than girls are born. The deathrate, moreover, among the boys is greater than among the girls during the first years of infancy, so that at the age of about 20, there are as many men as women. The deathrate for men is subsequently also greater than for women, largely as a result of the added risks and strain associated with the vocational work of the men. The predominance of women in the higher age-groups becomes therefore very marked.

All these are facts. When it comes to an explanation of the circumstances we are, however, somewhat deficient in knowledge. We have not even exact data on the number of natural abortions and their sex ratio[1]). This, among other things, results from the fact that an early abortion can be hard to distinguish from a delayed menstruation and that, above all, the sex of the earliest abortions

[1]) On a material from the Carnegie Collection, *Tietze* has found 107.9 male foetuses and 100 female. Consequently, he assumes that all previous statistics are faulty and that the high proportion of males is due to mistaken diagnosis of sex. However, this cannot very well be the case in regard to the stillborn and the late abortions in, for instance, the 6th and 7th month of gestation, where the males are in a very large majority. It is more probable that Tietze's material is not representative. I am inclined to suspect that the specimens the doctor sent to the

is difficult if not impossible to determine. Various authors have therefore arrived at different conclusions when attempting to calculate the primary ratio of the sexes. *Tauber* [1923], for example, thus arrived at a figure of 109 : 100 for the primary sex ratio which, however, he himself considers too low. *Auerbach* [1912] reached a figure of 116 : 100, whilst *Wedervang* [1924], on material from Magdeburg, arrived at a sex ratio of 134 : 100. We do not, however, know why more male than female embryos are formed. On the other hand, we do know that two kinds of spermatozoa are developed; those which determine the male sex and those which determine the female. These must develop in similar numbers and it is therefore an enigma why the "male" spermatozoa have greater prospect than the "female" of fertilizing the egg. The only explanation it has been possible to find, is that the male spermatozoa have one X-chromosome less than the female, and consequently on the average, should weigh a little less. Opinions are divided on the part that is played by the spermatozoa and their capacity for movement in the race for the egg. Some investigations seem to indicate that the main body of spermatozoa are conveyed to the vicinity of the egg through the peristalsis in the female sex organ. It is, moreover, said that by reason of what is called reotaxis the spermatozoa have a tendency to swim against the current, and therefore reach the egg. *Roth* [1893][1]) had, however, already established that this phenomenon is due purely to mechanical causes. The paper by *Roth* seems to have been completely forgotten. His paper concerns the movement of bacteria against a current. Moreover, the paper was issued from an ophthalmological clinic. Therefore it seems quite reasonable that it was overlooked. If, without being able to see land, one were to find oneself in a current in the sea, it would not be realized that one was exposed to a current. For this to be realized, it would be necessary to fix attention upon an object that is not moving. On the assumption, however, that the spermatozoa were propelled in every direction in a thin, flowing layer of fluid they would, sooner or later, have their

museum were mostly from artificial abortions. Then the specimens would perhaps be more easily taken care of, but you cannot expect to have the same majority of males in them as you get in spontaneous abortions. Tietze says that "the great majority of abortions were unintentional" but he gives no figures on this important point. To obtain such figures should be extremely difficult.

[1]) I have had my attention drawn to Roth's work through an unpublished inquiry which was carried out by Dr. Carl Gustaf Lagergren 1936.

heads bumped against a surface. The tail would in this way be swung downwards and when thus they became free, they would propel themselves against the stream. There is, in other words, no valid reason for mention of that peculiar attribute, called reotaxis. A slight difference in weight should, in any case, enable the male spermatozoa to propel themselves rather more swiftly, and thus to reach the egg somewhat more often than the female. It is, however, far from proved that the difference in weight is sufficiently great to explain the primary sex ratio. It has thus far not been possible to prove this hypothesis by experiment. One could, however, conceive of the idea of dividing up the spermatozoa after letting them race against a stream or centrifuging them and then using different parts for artificial insemination. No such experiment has as yet been carried out. It should not, however, meet with insuperable obstacles if applied to animals. The hypothesis can so far be regarded as perfectly reasonable. It should, however, be emphasized that the chromosomes are difficult to observe in a human being, and it is therefore uncertain if the spermatozoa which determine the male sex have one chromosome less than those which determine the female sex. The general opinion, at present, is that the "male" spermatozoa have the same number of chromosomes but only one X-chromosome, and corresponding to this, one Y-chromosome which, however, is smaller. The difference in weight between the "male" and "female" spermatozoa cannot, however, be of any great significance. It is therefore doubtful whether the foregoing hypothesis is correct.

The second question that arises is why the male embryos are found among abortions to a far greater extent. *Lenz* [1923] has presented a hypothesis which for the present has become the generally accepted explanation. He has pointed out that the so-called lethal factors in the sex chromosome assert themselves in the male embryos but not in the female. This must entail death and abortion to a greater extent in the case of the male embryo than in that of the female.

In contrast to this theory it can, however, be said that the lethal factor disappears through the selection to which it becomes subjected. As demonstrated by Sköld, they must reduce by half with every generation. It must therefore be assumed under such circumstances, that the lethal factor arises through the very high frequency of mutations in the sex chromosome which appears, however, unlikely, in view of what is known about the frequency of mutations in

general. It should further be remembered that the human being has in haploid dose 23 chromosomes, in addition to the sex chromosome or Y-chromosome. If lethal factors occur with the same frequency in these chromosomes, as in the sex chromosome, the former would soon become so charged with the lethal factors that new mutations of lethal factors would bring about an unreasonably high frequency of abortions. It therefore becomes necessary to supplement *Lenz'* contention with the assumption that lethal factors in the remaining chromosomes do not arise in anything like the same frequency as in the sex chromosome. An incredibly high mutation frequency which is limited to the sex chromosome, must then be postulated.

The deathrate during the first year of infancy is higher among boys than among girls. One is apt to associate this with the surplus deathrate for boys that occurs among the abortions. If this were to depend on lethal factors, or rather semi-lethal factors, one would expect that a disparity in the causes of death after birth would show itself between boys and girls. No such disparity exists, since the causes of death are approximately the same in both newborn boys and girls. This seems to indicate that the deathrate after birth is of a possibly different character from that of abortions. Besides, it would be strange if the mutations of lethal factors occurred in the sex chromosomes in so great a number, as there are not so many other mutations in the sex chromosome that are known. It is therefore hardly likely that *Lenz'* theory explains the whole of the surplus deathrate, but only a smaller part of it.

As the position is so unsatisfactory I should like to put forward a new hypothesis which has the advantage of explaining both problems. Both female and male spermatozoa have the same likelihood of fertilizing younger eggs, but if the probability of fertilizing older eggs is greater in the case of the male, it may conceivably explain not only the differing primary sex ratio but also the higher frequency of abortions in male embryos. It is thus reasonably credible that eggs which commence to grow old give rise to abortions if they are fertilized. There are some experimental investigations which support this hypothesis.

Richard Hertwig [1911], in his day, carried out with his pupils an experiment with frogs' eggs, and was able to demonstrate that eggs which were fertilized, when becoming somewhat old, gave rise principally to male embryos. All were male embryos in so far as it

concerned very old eggs. This investigation attracted great attention at the time but was ultimately forgotten when it became known that the sex was determined by the X-chromosome, and that the age of the egg could not, in itself, exert any influence on the sex. This, however, accords with my theory that old eggs are fertilized mainly by "male" spermatozoa. It is, in reality, the only credible explanation so long as no doubt is cast on the experiment which, since it was carried out by such a trained experimental biologist as *Richard Hertwig*, should be out of the question. He discusses various possibilities to interpret the result and seems to tend towards the theory that an X-chromosome is ejected by the fertilized egg. He then also must assume that the female sex is heterogametic which has been shown not to be the case.

Shortly before the outbreak of the second world war some experiments were undertaken in America indicating that old eggs which become fertilized result in abortions to a proportionately greater extent. Such experiments were carried out by *Blandau* and *Young* [1939] on guineapigs. *Blandau* and *Jordan* later [1941] carried out the same experiment on rats, with similar results. No further research has been undertaken, as far as I have been able to discover. The investigations that have thus far been made, have been carried out on much too small a number of animals for the purpose of solving the question of the sex ratio, in the case of old fertilized eggs. The experiments on guinea-pigs resulted in 99 living animals with a sex ratio of $51.1 \pm 5.3\,\%$ guinea-pigs of male sex. The sex among abortions is not given. These experiments, having regard to the large margin of error, could not be regarded as having proved anything. The experiments on rats resulted in 128 offspring with a sex ratio of $53.9 \pm 4.4\,\%$ rats of male sex. The controls showed $49.5 \pm 3.5\,\%$ of male sex. The difference, in other words, was far from statistically significant. More extensive material is required if proof is to be established.

Both investigations show, moreover, an increased frequency of abortions where the fertilization of old eggs takes place. The embryo becomes, in fact, often degenerated and more or less completely absorbed.

Even if the sex of all mammals is mainly determined in the same manner as in the case of human beings, there is evidence of certain differences of importance. It should be pointed out, in connection with the above-mentioned experiments, that heat in animals occurs

at a time when the egg is matured and discharged. When the period of heat is over, coitus is not permitted by the female animal. These experiments are therefore carried out by artificial insemination at such time as the heat begins to disappear.

Heat does not occur in the case of human beings and coitus can therefore take place at any time. This means that the prospect of old eggs becoming fertilized is only to be found in human beings, entailing an abnormal primary sex proportion and an abnormal frequency of abortions in accordance with the theory advanced. Corresponding phenomena are unlikely to be found among animals and this seems to be confirmed from information at our disposal.

The ratio of the sexes on the whole indicates that it is chance which is the factor determining the sex of the sperm that fertilizes the egg. Certain unexpected variations have, however, been found, as a result of carefully prepared statistical revisions on the basis of more extensive material. It is above all the Italian statistician, *Corrado Gini*, in particular, who dealt with this problem. He has for this purpose used the material collected by *Geissler*, comprising some 5 million births. *Gini* has shown that in families where they beget only boys, or only girls, the probability of giving birth in the former case, to a boy, or in the latter case, to a girl, in continuity, is somewhat increased. This variation is, however, slight and probably depends on the specially marked tendency in some women for old eggs to become fertilized. Such women consequently have a somewhat greater likelihood of giving birth to boys. It is conceivable that the reverse can occur, which means that women in whom the tendency for old eggs to become fertilized is not marked, have a relatively greater likelihood than usual of giving birth to girls. The variations in question are, as previously emphasized, quite insignificant, and mainly of theoretical interest.

In conclusion, it should be pointed out that by this hypothesis one replaces two others that are scarcely credible. If the experiment of Hertwig and his pupils is disregarded, there is no reason for assuming that old eggs, in particular, can be fertilized mainly by male determining sperms.

Summary.

The author discusses the difference between the primary sex ratio and the sex ratio at birth. The hypothesis is advanced that the

difference is due to most of the old (overripe) ova being fertilized by predominantly male determining spermatozoa and that this also explains why abortions are mostly male.

Résumé.

Discussion sur la différence entre la proportion sexuelle primaire et la proportion sexuelle à la naissance. L'hypothèse est présentée que la différence dépendrait des oves vieux (trop mûrs) étant fécondés principalement par des spermatozoïdes déterminant genre masculin. Cette hypothèse expliquerait aussi pourquoi les avortements sont surtout masculins.

Zusammenfassung.

Der Verfasser bespricht den Unterschied zwischen der primären Verteilung der Geschlechter und deren Verteilung bei der Geburt. Er stellt die Hypothese auf, daß der Unterschied darauf beruht, daß die meisten alten (überreifen) Eier von hauptsächlich männliches Geschlecht bestimmenden Spermazoen befruchtet werden; dies erklärt auch, warum Mißgeburten meistens männlichen Geschlechtes sind.

LITERATURE

Auerbach, E.: Archiv f. Rassen- u. Gesellschaftsbiol. *9*, 1912. – *Blandau, R. J.* and *E. S. Jordan:* Amer. J. Anat. *68*, 276, 1941. – *Blandau, R. J.* and *W. C. Young:* Amer. J. Anat. *64*, 303, 1939. – *Geißler, A.:* Zschr. d. K. Sachs. statist. Bureaus, 1889. – *Geißler, A.:* Allg. stat. Archiv, *IV*, 1896. – *Gini, C.:* Il sesso, dal punto di vista statistico. Roma 1908. – *Hertwig, Richard:* Biol. Zentralblatt *32*, 1, 1912. – *Lenz, F.:* Archiv f. Hygiene *93*, 1923. – *Mohr. O. L.:* Norsk Magazin f. Laegevidenskaben, Raekke 5, *14*, 77/1916. – *Roth, A.:* Dtsch. Med. Wschr. *19*, 351, 1893. – *Sköld, E.:* Haemophilia in Sweden and its treatment by blood transfusion. Inaug. Diss., Stockholm 1944. – *Tauber, R.:* Zschr. f. Geburtsh. u. Gynäk. *85*, 1923. – *Tietze, C.:* Hum. Biol. *20*, 156, 1948. – *Wedervang, I.:* Om seksualproportionen ved födselen, dens typer og disses variasjon med saerlig henblik på fosterdödeligheten. (Sex proportion and its variations in relation to ante-natal mortality.) Oslo 1924.

From the University Institute of Human Genetics, Copenhagen
(Chief: Tage Kemp, M. D.)

VITILIGO IN A PAIR OF MONOVULAR TWINS

by JAN MOHR

Introduction.

Comparison of monovular twin pairs with pairs of less closely related individuals, particularly binovular twins, may give information on the relative influence of heredity and environment on a given character. This has been utilized extensively in the study of normal as well as pathological traits.

The value of twin data in evaluating the influence of heredity and environment, is dependent upon our knowledge of the way in which the material was obtained. The ideal procedure would be to examine a random series of twin pairs with regard to the trait or disease in question; however, for practical reasons, this has been done only for the more frequent characters. Usually a twin material giving information on a disease is selected by the presence of this disease in one or both members of a twin pair; irrelevant factors, as the "oddity value" of the case, may also unfortunately play a role. A material of this kind is not ideal, but it appears valuable enough to justify the study and publication of even single cases of disease in twins; when a sufficient number of cases has appeared in the literature, they may be compiled and analyzed.

The present case of vitiligo was found accidentally in a series of twenty monovular twin pairs, which were studied with the structure of the iris as a main object.

An earlier report on vitiligo in twins.

A case of vitiligo in a pair of thirteen year old male twins has been described by *Schachter* (1947). Only one of the twins was affected. The anomaly was first noticed when the spouse was four years old. Gradually the defect developed further until, at the time of examination, the patches of deficient pigmentation covered most parts of the body. *Schachter* found hyperhidrosis, a mild degree of

exophtalmus and a basal metabolism of 125% in the twin with vitiligo, but not in the twin with normal skin. However, a significant relation between these traits and vitiligo remains unproven.

In *Schachters* case the diagnosis of monovularity was made by the fingerprints, eyecolor, shape of teeth and ears and by other anatomical characteristics; the twins are stated to look very much alike.

The present case.

Family. The *mother* of the twins with vitiligo is born 19. 9. 1905. The twins are her only children. According to her husband she shows in the summer, when tanned, patches of skin with deficient pigmentation around the mouth. These patches are not hypersensitive to sun light, as are the vitiligo spots of the twins. When examined in January 1951, she had, about twenty millimeters in front of the left ear, a patch of weakly pigmented skin. It measured about twenty millimeters across, the boundary was irregular in shape, and not very sharp. The depigmentation appeared to be far from complete; the hairs on the patch were of normal color, and not white as those on the patches of her sons. Otherwise the skin appeared normal. The second upper incisives and the upper right canine showed small white spots.

Serology: B, MS, Le(a—), R_1R_1, pp, Lu(a—). She is a taster of phenylthiourea.

The *father* is born 16. 9. 1902. He has never experienced any pigmentary anomaly, and the skin appeared normal when examined.

Serology: O, MsMs, Le(a—), R_2r, P, Lu(a—). He is a taster of phenylthiourea.

Neither the mother nor the father can recall any case of pigmentary defect in their sibs or parents.

The patients. History. The twins O. and H., both males, were born 16. 2. 1930. Forceps was used on O., who was born one hour after H. Both had pertussis and later morbilli when six years old. H. had otitis media at seven, a commotio cerebri at eight years of age. At ten O. developed verrucae plantae, which were treated with radium.

The vitiligo appeared first in O. It was examined 3. 6. 1940 by the physician who checked the results of the treatment of the verrucae, about a month after the radium treatment. The patient had noticed the defect a few weeks earlier. According to the twins and their parents the pigmentary defects progressed gradually for two or three years; at the end of this period white scalp hairs, scattered among the normal ones, were observed. In the following seven years the vitiligo changed very little.

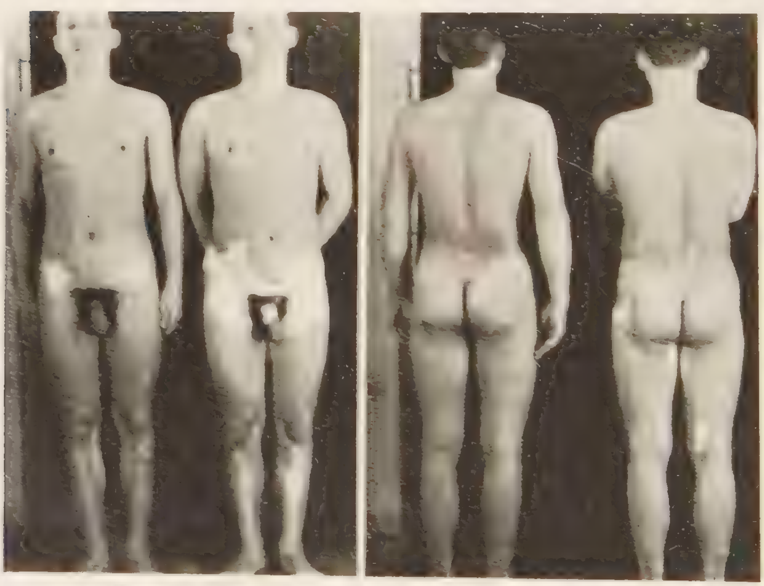
In H. the depigmentation appeared about two years later than in O., and it was always more moderate in extent.

The twins have had some discomfort from the hypersensitivity of the vitiligo patches to sun light. They have never been given any treatment for the skin anomaly.

Present state. Both twins appear to be in good health, and their physical development is good. They look very much alike (see photographs).

	O.	H.
Stature	[illegible] cm	171.8 cm
Hair shape	Straight	Straight
Hair color	Dark brown	Dark brown
Eye color	Light blue	Light blue
Iris structure [1]	K_0ac 0.2 ad 3	K_0ac 0.2 ad 3
Finger prints, ridge count	[illegible]	111
Serology	O, MS, Le(a—), R_1r P	O, MS, Le(a—), R_1r, P
Ability to taste phenylthiourea	Taster	Taster
Pigmentation of the skin	As the photographs show, the bulk of the depigmentation is in the pubic and inguinal regions; the skin on the root of the penis is affected. There are scattered spots in many regions of the body, on the legs particularly in the tibial and popliteal regions, on the arms in the cubital regions.	The area of depigmentation is only a fraction of that of O. It is mainly localized to the inguinal regions.
Pigmentation of hair	In the areas of depigmented skin, the lanugo is colorless. Part of the pubic hair is also depigmented. On the scalp there are scattered, single, completely depigmented hairs, among the normal ones.	As for O., except that the pubic and scalp hairs appear all normal.
Teeth	Normal	Normal

Fig. 1.



H O H O

[1] See [illegible] 19[illegible]

Probability of monovularity.

The estimated initial chance of like sexed twins being dizygotic is about 0.54: the chance of dizygotic twins in this family having the same ABO groups is 0.50 and the same Rhesus groups 0.50. These chances combined are 0.13. The relative chance of binovularity: monovularity is 0.13 : 0.46, the probability of monovularity 0.46 : $(0.46+0.13) = 0.77$. The identity of the MNS, *Lewis* and P groups in the two twins is additional evidence for monovularity. When this is combined with the anatomical data, which show a striking resemblance of the twins, the case for monovularity appears good.

Discussion.

The appearance of vitiligo in both members of a pair of probably monovular twins, at about the same age and with a somewhat similar localization, suggests that hereditary factors may influence the development of vitiligo. The pigmentary anomaly of the mother could be accidental; it might also be due to the same hereditary influence which, on another genetical background, as that of the twins, may give rise to a regular vitiligo. However, no other twin data giving support to the suggestion of a hereditary influence on this disease are known to the writer, and familial occurrence of vitiligo appears to be rare.

Summary.

A case of vitiligo in both members of a pair of monovular twins is described.

Résumé.

Description de vitiligo se montrant chez les deux membres d'un couple de jumeaux uniovulaires.

Zusammenfassung.

Beschreibung von Vitiligo in den beiden Mitgliedern eines eineiigen Zwillingspaares.

LITERATURE

Schachter, M.: Generalized vitiligo in one of uniovular twins. Ann. pœdiat. *169*, 337–344, 1947. – *Eskelund, V.:* Structural Variations of the Human Iris and their Heredity. H. K. Lewis & Co. Ltd. 136. Gowerstreet, London 1938.

ON THE MARGINAL ALVEOLAR RIDGE IN STUDENTS

A Rœntgenographic Study

by GUSTAF HERULF

In order to determine whether morbid processes are present in a given case, one must know what is normal. Obviously, the disease may be so advanced that there is no doubt concerning the existence of the changes. It is in the large number of borderline cases, that are difficult to diagnose clinically, that it is essential to know what may be considered normal for a given person at a given age.

This being so various criteria may be set up regarding, for example, such things as the interdental bony septa. It may be said that the person in whom they remain unchanged far into advanced age represents the ideally normal in this respect. Perhaps no such person actually exists: the interdental septa are known to shrink with age, although in a number of cases no disease can be found. Of course, this is an *a priori* presumption of a normal concept, and in practice that is perhaps what usually is done as there is no empiric research to fall back upon.

However, when it is desired to arrive at an empiric concept of what is normal, certain difficulties arise. As mentioned in the foregoing, the bony interdental septa usually atrophy in man as he grows older. This must be considered normal in so far as it is characteristic of most human beings, even if they feel healthy and live under what we like to think are normal conditions. In this sense of the term it is possible to know what is normal without examining a great number of healthy persons. But which persons are healthy? As a matter of fact, no one grows up in an environment without bacteria, the symptoms may develop surreptitiously, and may have very benign disorders. Strictly speaking it is impossible to define what is meant by a healthy person. Under doubtful conditions it might be feasible to operate with two or more degrees of healthiness with more or less restrictive health criteria. One could then investigate whether there was any difference between the different health groups in the factor

to be studied, e.g. the state of the mandible. Anyhow, it is obvious that one must distinguish between healthy and diseased persons in the most sensible way. Failing to use such a demarcation, one would set out from an *a priori* concept of the normal and merely move in a circle.

In the light of this fundamental reasoning it is not surprising that the interdental septa of diseased persons may be normal. A person who, for example, is afflicted with schiatica, can of course hardly for that reason have more deteriorated interdental septa than a healthy person. It may be assumed on the other hand, that diseases in the oral cavity and diseases that affect the general physical condition should be accorded the greatest attention when we have to consider structural conditions in the jawbone. Since little is yet known of how the general physical condition influences the state of the jaw, it is difficult to assess the importance of this factor. It might to all intents and purposes be eliminated as a troublesome source of error by selecting a series of persons for examination among whom maladjustments of the general physical condition are rare or not yet are likely to have had time to affect the structure of the jaw. From these points of view a series of comparatively young persons would perhaps be most suitable.

Also estimation of changes in the oral cavity meets with difficulties and thus gives rise to sources of error. Training and experience on the part of the observer materially facilitates the first rough sorting, but the closer one approaches the borderline between healthy and diseased, the more will the personal equation come into play. So, for example, there exists no universally accepted norm concerning the colour of the gingiva. Moreover, abnormal redness may be a very transient phenomenon. Estimates of the shape, consistency and position of the gingiva will, finally, vary slightly from observer to observer. Evidently quite a lot of difficulties present themselves, even if it were possible to find a series of test persons such that the rough sorting of healthy and diseased could be based on the state of the mouth.

It has just been hinted that a number of difficulties are met with in laying down norms for any observations that are made at an inspection. Nowadays, though, hardly any clinician neglects the opportunity of ascertaining the condition of the alveolar ridge by means of roentgenography. For such information is of the utmost importance when one has to decide on the therapy most likely to

aid the prevention of premature dedentition. The commonly accepted opinion is that protracted disorders of the gingiva in most cases are productive of changes in the jaw.

With access to a series of healthy normals—here to be understood in the sense of persons with apparently healthy gingiva—showing that the margin of the alveolar ridge ought to be a given distance away from the enamel edge at a given age, it would be possible to judge whether the jawbone were more atrophied in an individual case than it properly should be in view of the person's age. In order to eliminate any misunderstanding on this point, I should like to emphasize that the diagnosis cannot be set merely by such an analysis of the roentgenographic measurements. It might on the other hand be valuable, if by so doing one could establish some sort of norm to aid in estimating the extent of the jaw lesions. The literature in this field is very abundant with respect to etiology, pathogenesis and symptoms of the marginal disorders. These problems, however, will not be discussed in the present paper. Not being aware of any earlier systematic studies on the conditions of the jawbone, as they are portrayed roentgenographically, the author here merely wishes to contribute to the question of what may be considered normal concerning the level of the marginal alveolar ridge in a certain age class.

The test series was initially utilized to determine the reliability and value of various roentgen projections when it is required to obtain an image that as closely as possible portrays actual conditions.

Test Subjects.

Practically all students enrolled at the Institute of Dentistry from 1939–1946 declared themselves willing to participate. The mean age was 24.2 years and the age distribution will be seen in table 1. As all the separate test persons were examined at the same phase of their studies, the ages varied within a fairly small range at the time of observation. Thus, 80 per cent of the women and 60 per cent of the men were between 20 and 24 years old.

With respect to the actual conditions of the jaws, a limited part only was studied. It is probably a general experience which often is stressed in the literature, that caries, fillings and various types of prosthodontic structures tend to render the marginal jaws abnormal. Therefore, if it is desired to study the normal effect of aging on the jaws, parts of them should be selected where factors of this type are

Table 1. Age distribution.

Age, years	State of the gingiva Normal		Abnormal		Total	
	Number	Per cent	Number	Per cent	Number	Per cent
			Men			
< 20	—	—	—	—	—	—
20–24	107	64.5	122	54.8	229	58.9
25–29	53	31.9	79	35.4	132	33.9
30–34	2	1.2	9	4.0	11	2.8
35–	4	2.4	13	5.8	17	4.4
Total	166[1])	100.0	223	100.0	389[1])	100.0
			Women			
< 20	1	0.8	—	—	1	0.5
20–24	109	83.1	64	76.2	173	80.5
25–29	16	12.2	17	20.2	33	15.3
30–34	1	0.8	1	1.2	2	0.9
35–	4	3.1	2	2.4	6	2.8
Total	131[1])	100.0	84	100.0	215[1])	100.0

[1]) + 1 case without information in regard to age.

least frequent and which consequently are most nearly normal With these considerations in view the anterior mandible should yield the most reliable results; and we have accordingly confined our attention to the septa between the incisors in the lower jaw. Another factor contributed to this limitation, viz. examination of all the interdental septa would have involved so much work and taken so much time that a result could not have been produced within a reasonably short period.

The usual data as regards past diseases and present health were obtained, practically all the subjects declaring themselves fully fit at the time of examination. Some test persons were rejected, however, owing to previous operative intervention in the mandible, e.g. extractions and marginal surgery. In some other cases the test persons had had such previous diseases that he or she could not reasonably be included among a series of normals.

Data were also recorded concerning a number of other circumstances that here and there in the literature have been assumed to affect the state of the jaws. Thus, it was enquired of the students whether their pre-school life had been spent in an urban or in a rural environment; whether they actively participated in some competitive sport or athletics, just exercised a fair amount, or had no special

interest in bodily fitness; and whether they were smokers. The smokers were subdivided into three groups: "mild" smokers, consuming 1–5 cigarettes daily; "moderate" smokers, with 6–10 cigarettes daily, and "heavy" smokers, who took more than 10 cigarettes per day. Only those who had smoked consistently for at least 1 year were classified as smokers. The consumption of pipe and cigar tobacco was approximately converted into cigarette consumption.

The clinical inspection concerned the condition of the gingiva with respect to colour, shape, consistency and level in relation to the teeth; the position and occlusion of the teeth, and the consistency and colour of any dental deposits.

Finally, in 121 cases, the caries index was computed according to the method commonly adopted at the Institute of Dentistry, which method sets out from 100 free tooth surfaces. This clinical caries index was then related to the same person's caries index as computed by analyzing only the roentgenographs. I shall take the liberty, however, of presenting the result elsewhere.

Roentgen Technique.

For the purposes of this paper two roentgenographic methods were used, viz.

1. The ordinary method, based on the bisector theorem and here called the apical method.

2. The method of parallelling the film and the tooth and directing the beam of roentgen rays against the neck of the tooth which entails certain advantages. This method has been called the collum method.

Table 2. Comparison between the figures for the level of the septum in the same persons at collum projection, respectively apical projection.

Septum	Collum projection Number	$M \pm \varepsilon$ (M)	σ	Apical projection Number	$M \pm \varepsilon$ (M)	σ
		Cases with normal gingiva				
2–1–	193	0.961±0.032	0.446	183	0.733±0.029	0.398
1–1	266	1.220±0.031	0.511	258	0.940±0.030	0.486
–1–2	211	1.001±0.032	0.458	175	0.752±0.029	0.384
		Cases with changed gingiva				
2–1–	196	1.247±0.052	0.735	190	1.018±0.049	0.682
1–1	268	1.523±0.046	0.751	264	1.258±0.048	0.773
–1–2	226	1.294±0.046	0.688	213	1.010±0.046	0.676

It was found by comparing 500 roentgenographs taken with the aid of either method that there is a statistically significant difference. (Table 2.). The distance is about $^1/_3$ mm longer on the collum pictures than on the apical pictures. The apical pictures might be characterized by saying that they correctly reproduce the overall length of the tooth but distort the proportions between its parts. The pictures become apically elongated and coronarily compressed. By investigating how the pictures varied (table 3) it was found that the mean error of the collum method, when used by different operators, is smaller. This method is therefore preferable.

Table 3. **Double determinations of the septum levels.**

Septum	Number $= n$	Measurement carried out by The author $= M_1$	The assistant $= M_2$	$\frac{M_1+M_2}{2} = M_3$	Error of measurement $= \sqrt{\frac{\Sigma d^2}{2n}} = \sigma_i$	σ_i in per cent of M_3
		Collum projection				
–2 – 1	16	1.08	1.15	1.12	0.11	9.8
–1...1–	20	1.49	1.51	1.50	0.10	6.7
2 – 1–	12	1.23	1.16	1.19	0.14	11.8
		Apical projection				
–2 – 1	15	1.05	1.06	1.05	0.11	10.5
–1...1–	20	1.17	1.19	1.18	0.26	22.0
2 – 1–	11	1.02	0.98	1.00	0.13	13.0

The Pictorial Measurements.

Here it should be stressed that both the approximal enamel edge and the septal edge viewed from the approximal side have a contour that in the incisal direction may be convex in the form of a more or less vaulted arch, or it may be rather angular with a rounded apex.

If now the beam strikes the collum at right angles to the dental axis, the points on the bony and enamel margins closest to the incisal edge will probably be projected as the most appropriate point of reference for measuring the distance between the enamel and mandibular margins.

If, on the other hand, the beam strikes at an angle from above or below, parts other than topmost points of the enamel and bone margins, respectively, will probably be projected as septum and

enamel borders. Supposing that the edge of the bone and the enamel usually are parallel, then the latter direction of the beam would make no difference in the projection, as the distance between corresponding points on the real contours would remain the same. This matter cannot be definitely cleared up without recourse to a large post-mortem series. The author knows of no previous study on this problem and has not been able to undertake one himself. Here it must suffice to remind of the following facts.

The consistent and significant difference in this series between the septal measurements as taken by the apical method and by the collum method may perhaps partly be due to a projection of non-corresponding parts of the two contours as enamel and bone margins, respectively. The previously mentioned compression of the "apical" image, owing to the angle between the tooth and root planes, may also have something to do with it. However, we can only state that, with respect to such sources of error, the collum pictures should in principle be superior to the apical pictures. The adjacent, approximal enamel margins of neighbouring teeth were inspected through a magnifier and the point of reference marked with a pin prick. So was the topmost point on the septum. When the shape of the septum was normal this was an easy matter. Sometimes, however, the septum had a more horizontal contour: sometimes disease had caused it to lie lower at one root than at the other. When the septal contour was slightly convex or horizontal its midpoint was taken as the point of reference. When it was sloping two points of reference were used: the highest and lowest point on the contour, the mean being used in the numerical analysis.

In the present investigation the *level of the interdental septum* with reference to the enamel margin was taken as: the perpendicular distance between the points of reference on the two adjacent enamel margins and the aforementioned reference point(s) on the septal contour.

It occasionally happened that a reference point was blurred and therefore the number of observations for central septa and for side septa do not always agree in the tables.

There being no significant or probable difference (cf. table 4) between pairs of side septa, the two were combined for some analyses.

The measurements were taken under a magnifier with a pair of specially made dividers that were graduated in tenths of a millimetre.

Ordinary odontological X-ray equipment was used and the processing of the films was standardized.

Table 4. Position of the septal levels on the right side, respectively on the left side.

Conditions of the gingiva	Septum 2 – 1 – Number	M ± ε (M)	σ	– 1 – 2 Number	M ± ε (M)	σ
		Collum projection				
Normal	193	0.961±0.032	0.446	211	1.001±0.032	0.458
Changed . . .	196	1.247±0.052	0.735	226	1.294±0.046	0.688
		Apical projection				
Normal	183	0.733±0.029	0.398	175	0.752±0.029	0.384
Changed . . .	190	1.018±0.049	0.682	213	1.010±0.046	0.676

Classification and Analysis of Observations.

The observed test persons comprised, as we have seen in the foregoing, subjectively healthy students at the Institute of Dentistry. However, the absence of general symptoms does not prevent a person from having diseases affecting the teeth and jaws. Sometimes such disorders might even be present without definite local symptoms.

How, in order that the analysis shall provide the most information, should the observations be grouped?

It may be assumed that in the majority of cases the morbid processes giving rise to changes in the marginal bony tissues make themselves known as symptoms in the gingiva, e. g. gingivitis, hypertrophy, etc.

Hence, the series was first classified into two main groups:

I. Persons with normal gingiva, and

II. Persons with abnormal gingiva.

The condition of the gingiva was judged according to colour, consistency (spot pressure resilience), secretion, if any, expressed by pressure over a larger area, and shape and level in relation to the teeth.

Whether or not the gingiva is normal is often plainly evident. There are always borderline cases, however, and then the problem may be rather difficult. In such cases the subjectiveness of different observers will obviously be of greater importance than in the plain cases. The object being to select a series of normals with respect to hard tissue roentgenography and, as pointed out in the foregoing,

since bone and gingiva changes usually seem to coexist, no in the author's opinion doubtful cases were included in the normal group. Hereby the second group might appear to be better than it actually is.

A number of fundamental factors, which by various early and recent authors are assumed to affect the jaw, were analyzed in these two main groups.

The factors were as follows:

1. Presence of deposits, their consistency and localization.
2. Arrangement of the teeth.
3. Smoking habits.
4. Environment during growing period.
5. Interest in exercise.
6. Roentgenographic appearance of jaw: the main theme of the present study.

The surprising fact evolved from the classification of the series into two groups, according to the condition of the gingiva, that the number of persons with normal gingiva was approximately the same as the number of persons with abnormal gingiva.

It appeared, regarding the sex distribution, that 56 per cent of the men and 39 per cent of the women had more or less diseased gingiva (table 5).

Table 5. Distribution of the material with regard to the state of the gingiva.

State of the gingiva	Projection	
	Collum	Apical
Men		
Normal	155	144
Changed	199	199
Total	354	343
Women		
Normal	112	118
Changed	71	72
Total	183	190
Both sexes		
Normal	267	262
Changed	270	271
Total	537	533

Table 6. Frequency of cases with dental deposits distributed with regard to the state of the gingiva.

State of the gingiva	With dental deposits		Without dental deposits	
	Number	%	Number	%
		Men		
Normal	53	26.8	112	60.2
Changed	145	73.2±3.1	74	39.8±3.6
Total	198	100.0	186	100.0
		Women		
Normal	47	44.3	85	79.4
Changed	59	55.7±4.8	22	20.6±3.9
Total	106	100.0	107	100.0
		Both sexes		
Normal	100	32.9	197	67.2
Changed	204	67.1±2.7	96	32.8±2.7
Total	304	100.0	293	100.0

Clinical Results.

Deposits (table 6). Half the test persons had deposits, but in this respect there was no difference between the sexes. In the main group with normal gingiva $^1/_3$ of the test persons had deposits and so had $^1/_3$ of the persons in the other group with diseased gingiva. Evidently the existence of deposits to some extent parallels the presence of gingiva changes, which of course by no means is surprising. There being no difference between the sexes, it can hardly be said, on the basis of the selected series of test persons, that dental deposits are responsible for the greater frequency of gingiva changes in men. Smoking perhaps promotes the formation of deposits, but this test does not provide conclusive evidence.

Arrangement of Teeth (table 7). If the arrangement of the teeth could affect the frequency of gingiva changes, it is likely that jaws with normally arranged teeth would not exhibit gingiva changes as often as jaws with anomalous teeth. The figures show such a tendency which, however, is not statistically significant but may be due to random variation. When men and women are taken together, gingiva changes are present in 51 per cent of those with normally arranged teeth. Jaws with crowded teeth show gingiva changes in 58 per cent. The differenc e is 7.3±4.8 per cent.

Table 7. Frequency of cases with anomalous arrangement of teeth, distributed with regard to the state of the gingiva.

State of the gingiva	Arrangement of teeth					
	Normal		Crowded		Spaced	
	Number	%	Number	%	Number	%
			Men			
Normal	76	40.0	40	37.4	46	61.3
Changed . . .	114	60.0 ± 3.6	67	62.6 ± 4.7	29	38.7 ± 5.6
Total	190	100.0	107	100.0	75	100.0
			Women			
Normal	79	62.7	26	51.0	19	70.4
Changed . . .	47	37.3 ± 4.3	25	49.0 ± 7.0	8	29.6 ± 8.8
Total	126	100.0	51	100.0	27	100.0
			Both sexes			
Normal	155	49.1	66	41.8	65	63.7
Changed . . .	161	50.9 ± 2.8	92	58.2 ± 3.9	37	36.3 ± 4.8
Total	316	100.0	158	100.0	102	100.0

However, when spaced are compared to normal tooth arrangements, the resulting difference is contrary to the expected and equals 14.6 ± 5.6 per cent. Thus, it may be due to random variation.

It seems, in other words, as though in this age group the influence, if any, of dentition anomalies on gingiva changes is so slight as to be nonmeasurable.

Smoking Habits (table 8). Half the test persons were smokers: 59 per cent of the men and 35 per cent of the women. It was found that 61 per cent were smokers in the main group with diseased gingiva, while only 41 per cent did so in the group with healthy gingiva. This difference is statistically significant. Undoubtedly smoking brings on a proneness for gingiva changes.

The smokers were subdivided into three classes, according to their consumption, in the manner described above.

It will be seen from the table that the number of heavy and the number of moderate smokers are far greater among men than among women. This may conceivably be the reason why gingiva changes are more frequent in men: among non-smokers the sex difference in the frequency of gingiva changes is not statistically significant. Among men and women who smoke little the frequency of gingiva changes is about the same, the difference being $12.1 \pm 10,3$ per cent.

Table 8. Frequency of smokers distributed with regard to the state of the gingiva.

State of the gingiva	Heavy smokers		Moderate smokers		Light smokers		Total number of smokers		All observed cases	
	Number	%	Number	%	Number	%	Number	%	Number	%
					Men					
Normal	9	20.5	38	42.2	31	40.8	78	37.1	155	43.7
Changed	35	79.5±6.1	52	57.8±5.2	45	59.2±5.6	132	62.9±3.3	200	56.3
Total	44	100.0	90	100.0	76	100.0	210	100.0	355	100.0
					Women					
Normal	2	66.7	11	40.7	18	52.9	31	48.4	114	62.0
Changed	1	33.3	16	59.3±9.5	16	47.1±8.6	33	51.6±6.2	70	38.0
Total	3	100.0	27	100.0	34	100.0	64	100.0	184	100.0
					Both sexes					
Normal	11	23.4	49	41.9	49	44.5	109	39.8	269	49.9
Changed	36	76.6±6.2	68	58.1±4.6	61	55.5±4.7	165	60.2±3.0	270	50.1
Total	47	100.0	117	100.0	110	100.0	274	100.0	539	100.0

Possibly, therefore, the higher frequency of gingiva changes in men, as compared to women, is because men smoke oftener and more heavily. It is not absolutely out of the question that there would be a difference between the sexes in the non-smoking group, if a much larger series were available, but nothing indicates that it would be very large. Consequently, it may be stated with great confidence that the chief reason why women have healthier gingiva than men is that they smoke less.

Childhood Environment (table 9). It has sometimes been suggested that a childhood spent in the country probably would lay the foundation for a better physique than that possessed by genuine children of the city. We therefore queried the test persons on this matter; the replies would be true at least as regards the place of birth, though the person might have been moved during pre-school age and therefore not grown up in the same environment into which he was born. Naturally such information may be somewhat unreliable. Anyhow, the figures show no significant differences and no deviation.

Exercise (table 10). This too is a factor that may be mentioned here and there as conducive to fitness and health. In this respect the investigation produced no significant differences in the condition of the gingiva between those who led a sedentary life and those who took

Table 9. Distribution according to childhood environment (town or country) and state of the gingiva.

State of the gingiva	Town Number	Town %	Country Number	Country %	All cases Number	All cases %
			Men			
Normal . . .	86	51.5±3.9	81	48.5±3.9	167	100.0
Changed . .	135	60.5±3.3	88	39.5±3.3	223	100.0
Total	221	56.7±2.5	169	43.3±2.5	390	100.0
			Women			
Normal . . .	84	63.6±4.2	48	36.4±4.2	132	100.0
Changed . .	60	71.4±4.9	24	28.6±4.9	84	100.0
Total	144	66.7±3.2	72	33.3±3.2	216	100.0
			Both sexes			
Normal . . .	170	56.9±2.9	129	43.1±2.9	299	100.0
Changed . .	195	63.5±2.7	112	36.5±2.7	307	100.0
Total	365	60.2±2.0	241	39.8±2.0	606	100.0

exercise. In this connection it is worth while mentioning that studies on large groups of conscripts in the Northern Countries have yielded very depressing results as regards gingiva conditions.

* * *

Table 10. Frequency of individuals interested in exercise, respectively competitive sports, distributed with regard to the state of the gingiva.

State of the gingiva	Interested in exercise Number	Interested in exercise %	Interested in competitive sports Number	Interested in competitive sports %	Not interested in exercise Number	Not interested in exercise %	All individuals Number	All individuals %
				Men				
Normal . .	93	56.4±3.9	56	33.9±3.7	16	9.7±2.3	165	100.0
Changed .	111	52.6±3.4	77	36.5±3.3	23	10.9±2.1	211	100.0
Total . . .	204	54.2±2.6	133	35.4±2.5	39	10.4±1.6	376	100.0
				Women				
Normal . .	92	74.8±3.9	16	13.0±3.0	15	12.2±3.0	123	100.0
Changed .	51	67.1±5.4	10	13.2±3.9	15	19.7±4.6	76	100.0
Total . . .	143	71.8±3.2	26	13.1±2.4	30	15.1±2.5	199	100.0
				Both sexes				
Normal . .	185	64.2±2.8	72	25.0±2.6	31	10.8±1.8	288	100.0
Changed .	162	56.5±2.9	87	30.3±2.7	38	13.2±2.0	287	100.0
Total . . .	347	60.3±2.0	159	27.7±1.9	69	12.0±1.4	575	100.0

With regard to the external factors studied here, which might influence the state of the gingiva, we may consequently state, by way of summing up, that smoking and the presence of dental deposits are the chief factors affecting the health of the gingiva.

Table 11. Tetrachoric coefficients of correlation between state of the gingiva and smoking respectively presence of dental deposits, and between dental deposits and smoking.

Sex	Number	$r \pm \varepsilon$ (r)
	Gingiva — Smoking	
Men	355	$+0.252 \pm 0.081$
Women	184	$+0.323 \pm 0.112$
Both sexes	539	$+0.318 \pm 0.063$
	Gingiva — Dental deposits	
Men	384	$+0.508 \pm 0.065$
Women	213	$+0.549 \pm 0.085$
Both sexes	597	$+0.514 \pm 0.052$
	Dental deposits — Smoking	
Men	349	$+0.024 \pm 0.085$
Women	181	$+0.14 \pm 0.12$
Both sexes	530	$+0.072 \pm 0.068$

In order better to appreciate these factors we have computed the tetrachoric correlation coefficient (table 11). In both sexes the correlation for smoking is 0.32 ± 0.06 and for deposits 0.51 ± 0.05. Both correlations are significant, which was to be expected. The difference between the deposit correlation and the smoking correlation is 0.20 ± 0.08 and is therefore neither significant nor even probable.

Another interesting point is whether smoking is correlated to the presence of dental deposits. It turned out, however, that there is no significant correlation for deposits, which might indicate that smokers are no more likely to get deposits than others. Probably, however, the series was not large enough.

Hence, the most important result of the clinical examination is the strong correlation prevailing between smoking and gingiva changes. It must be stressed, however, that our test persons were young and usually had not smoked very many years. Perhaps

habituation in time occurs so that smoking then no longer irritates the gingiva as much as in young smokers. In order to find out it would be necessary to study a series of older smokers.

Roentgenographic Results.

The normal septum has often been assumed *a priori* to lie on the level of the alveolar ridge in relation to the teeth. By so doing any reduction of the interdental septa will obviously be considered pathologic.

If an attempt is made to clear up the matter empirically one will find that already at age 20 the septa appear to have shrunk. The question then arises, what is the cause of this reduction. Is it a symptom of some particular pathologic process or is it the result of normal atrophy for the age?

Before discussing this problem, we shall first review the empiric results for the two main groups of test persons: those with normal gingiva and those with diseased gingiva.

Considering first the values for the normal group (table 12), we find that the mean level of the septum between the two first mandibular incisors is 1.2 mm below the enamel-cementum junction. The septa between the first and the second incisor on either side have a level somewhat closer to the enamel-cementum junction, i.e. 1.0 mm away from it. These figures apply to *men*.

In the *women* we find the corresponding values for the central septum 1.3 mm and for the side septa 1.0 mm. Here should be pointed out that the difference in height between the central septum and the side septa for men and women agree with this as given in table 13.

We find also that the variability is about the same in the two sexes. Women show a tendency to a greater difference in level, but the difference is not significant. In the following we have combined the values for men and women in order to increase the scope of our observations.

Coming now to the *group with gingiva changes* (table 12), we find in respect of the *men* that the mean level of the middle septum lies 1.6 mm below the enamel-cementum junction, and that the corresponding figure for the side septa is 1.3 mm. The corresponding means for *women* are 1.4 and 1.2 mm. The women consistently showed a tendency to higher septa than the men, but the deviation

Table 12. Levels of the septa between different teeth in cases with normal and with abnormal gingiva at collum projection, respectively apical projection. Comparison between men and women.

Septum	Men			Women		
	Number	M ± ε (M)	σ	Number	M ± ε (M)	σ
			Cases with normal gingiva Collum projection			
2–1–	111	0.945±0.043	0.456	82	0.982±0.048	0.431
1–1	154	1.160±0.042	0.516	112	1.301±0.046	0.492
–1–2	119	0.972±0.042	0.456	92	1.039±0.048	0.458
			Cases with abnormal gingiva Collum projection			
2–1–	144	1.266±0.067	0.799	52	1.196±0.071	0.514
1–1	197	1.562±0.058	0.807	71	1.414±0.065	0.552
–1–2	164	1.315±0.059	0.752	62	1.239±0.060	0.473
			Cases with normal gingiva Apical projection			
2–1–	101	0.732±0.043	0.437	82	0.734±0.038	0.346
1–1	141	0.907±0.043	0.510	117	0.979±0.042	0.451
–1–2	93	0.729±0.043	0.419	82	0.778±0.037	0.339
			Cases with abnormal gingiva Apical projection			
2–1–	135	1.032±0.062	0.721	55	0.984±0.077	0.574
1–1	193	1.272±0.059	0.825	71	1.220±0.073	0.612
–1–2	154	1.019±0.057	0.712	59	0.986±0.074	0.572

may have been due to random variation. *For both sexes combined all three septa differed significantly from their counterparts in the group with normal gingiva, independently of whether the collum or the apical projection was used.*

We have in the foregoing reviewed some classifications of the test persons with respect to certain clinical aspects, such as smoking

Table 13. Comparison between septum 1–1 and 1–2 at orthoradial direction of the beam against the respective septa and the same plate position.

Septum	Number	Mean at orthoradial direction of the beam against		Individual differences arising at different directions of the beam	
		Central septum = A	Side septum = B	D ± E (D)	σ (D)
–1–2	21	0.952	1.085	—0.133±0.074	0.341
1–1	21	1.300	1.200	0.100±0.046	0.210

habits, dental deposits, etc. A special analysis of the state of the interdental septa in these special groups was carried out. The following is a review of the values obtained thereby.

Dental Deposits (table 14). In persons with deposits the mean difference of all levels is consistently higher than in persons without deposits. In the main group with *normal gingiva* probable differences

Table 14. Levels of the septa in cases with and without dental deposits irrespective of sex.

Septum	Cases with dental deposits			Cases without dental deposits		
	Number	$M \pm \varepsilon$ (M)	σ	Number	$M \pm \varepsilon$ (M)	σ
Cases with normal gingiva. Collum projection						
2–1–	63	0.997±0.060	0.477	129	0.944±0.038	0.430
1–1	83	1.340±0.059	0.537	181	1.167±0.036	0.489
–1–2	70	1.126±0.057	0.478	139	0.940±0.037	0.436
Right + left	133	1.065±0.042	0.482	268	0.942±0.026	0.433
Cases with abnormal gingiva. Collum projection						
2–1–	123	1.254±0.065	0.719	69	1.235±0.090	0.751
1–1	174	1.552±0.057	0.755	88	1.470±0.078	0.732
–1–2	150	1.329±0.058	0.712	72	1.251±0.075	0.637
Right + left	273	1.296±0.043	0.716	141	1.243±0.059	0.695
Cases with normal gingiva. Apical projection						
2–1–	66	0.782±0.062	0.502	116	0.709±0.030	0.322
1–1	88	1.070±0.061	0.571	169	0.871±0.032	0.420
–1–2	63	0.814±0.058	0.462	111	0.717±0.031	0.329
Right + left	129	0.798±0.043	0.483	227	0.713±0.022	0.326
Cases with abnormal gingiva. Apical projection						
2–1–	126	1.033±0.060	0.677	60	0.975±0.088	0.680
1–1	175	1.274±0.058	0.767	85	1.206±0.085	0.783
–1–2	138	1.081±0.060	0.700	71	0.889±0.073	0.614
Right + left	264	1.058±0.042	0.689	131	0.928±0.057	0.647

are found in this respect for, on the one hand, the middle septum and, on the other, for both the left side septum as well as for the two side septa combined. For those who lack dental deposits the midseptal level is about 1.2 mm and the side-septal level about 1.0 mm.

In the main group with *changed gingiva* the persons without dental deposits had a mean middle septum value of 1.5 mm and a mean side septum value of 1.2 mm, but the corresponding values for the test persons with deposits were 1.6 mm and 1.3 mm.

It seems surprising that as many as about 80 of the test persons had deposits without showing inflammatory irritation or other signs of gingival changes, at the same time as their interdental septa were considerably reduced compared with the persons who also had normal gingiva but lacked deposits. However, we have here no reason to discuss the problems unfolded by this observation, e.g. the effect of the localization on the tooth of the deposit, and the organisms that in different instances occur together with the deposit, respectively the possibility of individual differences in the resistance of the gingiva.

Dental Arrangement (table 15). The septal height was not as affected by different dental arrangements as we have found to be the case by smoking and deposits.

Table 15. Levels of the septa in cases with different dental arrangements irrespective of sex.

Septum	Dental position: Normal			Crowded			Spaced		
	Number	$M \pm \varepsilon$ (M)	σ	Number	$M \pm \varepsilon$ (M)	σ	Number	$M \pm \varepsilon$ (M)	σ
Cases with normal gingiva. Collum projection									
2–1–	110	0.946±0.046	0.478	36	1.067±0.066	0.396	40	0.880±0.055	0.348
1–1	138	1.217±0.031	0.370	57	1.274±0.077	0.579	61	1.131±0.063	0.493
–1–2	115	0.981±0.042	0.451	32	1.188±0.092	0.518	56	0.907±0.052	0.387
Right + left	225	0.964±0.031	0.465	68	1.124±0.055	0.454	96	0.896±0.038	0.370
Cases with changed gingiva. Collum projection									
2–1–	111	1.205±0.058	0.606	47	1.304±0.107	0.773	28	1.296±0.154	0.815
1–1	143	1.517±0.049	0.589	76	1.516±0.098	0.856	33	1.482±0.145	0.836
–1–2	128	1.254±0.050	0.563	54	1.446±0.110	0.807	31	1.148±0.121	0.672
Right + left	239	1.231±0.038	0.584	101	1.380±0.077	0.773	59	1.219±0.096	0.734
Cases with normal gingiva. Apical projection									
2–1–	99	0.746±0.041	0.411	35	0.837±0.068	0.401	41	0.627±0.056	0.361
1–1	135	0.927±0.040	0.459	55	0.991±0.064	0.471	57	0.911±0.071	0.536
–1–2	96	0.710±0.036	0.354	28	0.943±0.070	0.370	44	0.705±0.061	0.402
Right + left	195	0.729±0.028	0.384	63	0.884±0.048	0.385	85	0.667±0.041	0.380
Cases with abnormal gingiva. Apical projection									
2–1–	105	0.962±0.058	0.591	52	1.060±0.096	0.696	25	1.096±0.165	0.823
1–1	142	1.216±0.057	0.680	77	1.288±0.091	0.802	33	1.361±0.156	0.894
–1–2	119	0.971±0.054	0.591	56	1.102±0.103	0.769	28	0.996±0.138	0.731
Right + left	224	0.967±0.039	0.591	108	1.081±0.071	0.735	53	1.043±0.105	0.763

Here the most interesting group is the one comprising test persons with healthy gingiva. It reveals that the septal height is consistently lower when the teeth are crowded and higher when the teeth are far apart compared to normal. However, significant or probable differences do not exist between normal and anomalous teeth, but the opposite tendencies exhibited by the crowded and spaced arrangements is accentuated by a significant difference for the side septa in the other main group with abnormal gingiva.

Childhood Environment (table 16). Any appreciable deviations from the means for the entire series was not obtained in the test group with normal gingiva. It is remarkable, on the other hand, that one probable difference exists for the middle septum and two significant differences for the side septa when rural domicile during pre-school life was compared with urban. The city persons consistently had higher septa than the rural.

Table 16. **Septal levels in cases born in the country respectively in a city irrespective of sex.**

Septum	Born in a city			Born in the country		
	Number	$M \pm \varepsilon$ (M)	σ	Number	$M \pm \varepsilon$ (M)	σ
Cases with normal gingiva. Collum projection						
2–1–	112	0.998 ± 0.040	0.432	81	0.909 ± 0.052	0.471
1–1	150	1.237 ± 0.040	0.489	116	1.197 ± 0.050	0.536
–1–2	115	1.018 ± 0.042	0.448	96	0.981 ± 0.048	0.469
Right + left	227	1.008 ± 0.029	0.436	177	0.948 ± 0.035	0.471
Cases with changed gingiva. Collum projection						
2–1–	123	1.354 ± 0.075	0.829	73	1.067 ± 0.057	0.490
1–1	170	1.589 ± 0.063	0.825	98	1.408 ± 0.059	0.583
–1–2	139	1.363 ± 0.065	0.762	87	1.184 ± 0.057	0.530
Right + left	262	1.359 ± 0.049	0.794	160	1.131 ± 0.041	0.516
Cases with normal gingiva. Apical projection						
2–1–	110	0.725 ± 0.036	0.379	73	0.744 ± 0.050	0.426
1–1	148	0.924 ± 0.037	0.452	110	0.961 ± 0.050	0.527
–1–2	92	0.760 ± 0.038	0.366	83	0.743 ± 0.044	0.403
Right + left	202	0.741 ± 0.026	0.374	156	0.744 ± 0.033	0.414
Cases with changed gingiva. Apical projection						
2–1–	122	1.129 ± 0.067	0.742	68	0.819 ± 0.061	0.500
1–1	165	1.345 ± 0.064	0.824	99	1.111 ± 0.066	0.656
–1–2	131	1.073 ± 0.063	0.716	82	0.909 ± 0.066	0.594
Right + left	253	1.100 ± 0.046	0.729	150	0.868 ± 0.045	0.555

In the foregoing we have pointed out that a person who was born in the country may have grown up in a city, and vice versa. In other words the information is unreliable. It seems reasonable, though, that those who are born in the country have grown up there oftener than those who are born in an urban community. The difference is therefore interesting, but the question cannot be definitely settled until more reliable data are available.

Exercise (table 17). The classification under this heading shows that large groups took moderate exercise, while small groups either participated actively in competitive sports or avoided all unnecessary activity. The spreading of the deviations varies strongly and no significant differences were obtained nor could any definite tendency be discovered, but that was scarcely to be expected.

Table 17. Septal levels in cases interested in moderate exercise, respectively competitive sports, and in those not interested in exercise, irrespective of sex.

Septum	Exercise			Competitive sports			Not interested in exercise		
	Number	$M \pm \varepsilon$ (M)	σ	Number	$M \pm \varepsilon$ (M)	σ	Number	$M \pm \varepsilon$ (M)	σ
				Cases with normal gingiva. Collum projection					
2–1–	122	0.953±0.043	0.473	46	0.963±0.053	0.362	23	1.026±0.097	0.463
1–1	169	1.246±0.039	0.504	65	1.137±0.068	0.546	30	1.243±0.086	0.469
–1–2	131	1.051±0.041	0.464	52	0.902±0.056	0.405	25	0.952±0.100	0.502
Right + left	253	1.004±0.030	0.471	98	0.931±0.039	0.385	48	0.988±0.069	0.480
				Cases with changed gingiva. Collum projection					
2–1–	115	1.253±0.071	0.761	56	1.245±0.089	0.663	23	1.244±0.165	0.790
1–1	153	1.533±0.065	0.808	77	1.482±0.080	0.698	36	1.575±0.102	0.614
–1–2	130	1.302±0.065	0.743	63	1.217±0.073	0.583	32	1.400±0.114	0.646
Right + left	245	1.279±0.048	0.752	119	1.230±0.057	0.622	55	1.335±0.095	0.707
				Cases with normal gingiva. Apical projection					
2–1–	109	0.734±0.040	0.413	48	0.754±0.059	0.412	18	0.689±0.077	0.327
1–1	158	0.934±0.037	0.464	64	0.913±0.071	0.569	25	1.084±0.084	0.419
–1–2	106	0.767±0.037	0.384	40	0.685±0.058	0.368	20	0.820±0.102	0.457
Right + left	215	0.750±0.027	0.399	88	0.723±0.042	0.390	38	0.758±0.065	0.401
				Cases with changed gingiva. Apical projection					
2–1–	101	0.932±0.061	0.609	52	1.037±0.090	0.651	21	1.038±0.165	0.757
1–1	135	1.156±0.062	0.724	76	1.283±0.085	0.744	34	1.359±0.137	0.798
–1–2	108	0.946±0.064	0.669	60	0.985±0.083	0.696	28	1.204±0.123	0.652
Right + left	209	0.939±0.044	0.641	112	1.009±0.061	0.649	49	1.133±0.099	0.696

Table 18. **Levels of the septa in smokers and non-smokers irrespective of sex.**

Septum	Non-smokers Number	Non-smokers $M \pm \varepsilon$ (M)	Non-smokers σ	Light smokers Number	Light smokers $M \pm \varepsilon$ (M)	Light smokers σ	Moderate smokers Number	Moderate smokers $M \pm \varepsilon$ (M)	Moderate smokers σ	Heavy smokers Number	Heavy smokers $M \pm \varepsilon$ (M)	Heavy smokers σ
Cases with normal state of the gingiva. Collum projection												
2–1–	116	0.957±0.037	0.395	30	0.937±0.079	0.433	37	0.970±0.096	0.581	10	1.040±0.169	0.534
1–1	158	1.199±0.035	0.441	49	1.249±0.079	0.551	48	1.242±0.088	0.610	11	1.291±0.239	0.792
–1–2	128	0.963±0.035	0.399	37	1.105±0.082	0.501	38	0.995±0.095	0.583	7	1.200	—
Cases with abnormal state of the gingiva. Collum projection												
2–1–	79	1.198±0.088	0.786	45	1.147±0.085	0.568	50	1.278±0.095	0.670	21	1.557±0.206	0.946
1–1	104	1.495±0.076	0.777	59	1.334±0.077	0.594	68	1.525±0.083	0.688	36	1.903±0.149	0.892
–1–2	91	1.241±0.065	0.622	51	1.143±0.069	0.492	55	1.287±0.097	0.720	28	1.743±0.177	0.935
Cases with normal state of the gingiva. Apical projection												
2–1–	94	0.714±0.035	0.340	28	0.736±0.086	0.456	29	0.721±0.090	0.487	9	0.700	—
1–1	136	0.899±0.035	0.411	41	0.941±0.093	0.596	43	0.940±0.083	0.545	8	1.075	—
–1–2	91	0.719±0.034	0.326	29	0.772±0.098	0.528	26	0.819±0.098	0.500	7	0.771	—
Cases with abnormal state of the gingiva. Apical projection												
2–1–	63	0.914±0.081	0.646	35	0.860±0.099	0.589	41	1.071±0.098	0.627	19	1.200±0.181	0.791
1–1	90	1.173±0.076	0.717	48	1.056±0.095	0.661	60	1.255±0.089	0.693	29	1.600±0.178	0.956
–1–2	74	0.927±0.066	0.563	40	0.855±0.095	0.599	48	1.046±0.101	0.698	21	1.338±0.213	0.976

Tobacco (tables 18 and 19). On the subject of smoking in relation to septal height we have found the following. The mean mid-septal value for smokers with *normal gingiva* was 1.25 mm. The values for the side septa lay around 1.0 mm, except in heavy smokers, where they attained 1.1 mm. No significant or probable difference existed between smokers and non-smokers in this group.

In the group with *diseased gingiva* the mid-septal values were respectively 1.3, 1.5 and 1.9 mm, for the three aforesaid degrees of smoking. The corresponding values for the side septa were 1.1, 1.3 and 1.7 mm. For the middle and one side septum there are significant differences between heavy smokers and non-smokers. A probable difference is obtained by comparing, on the hand, nonsmokers and mild smokers and, on the other, moderate and heavy smokers.

In the foregoing we have found a significant difference between the number of smokers (61 per cent) with changed gingiva and the number of smokers (41 per cent) in the normal group. Comparing now the septal height in these two groups of smokers, we find in the group with changed gingiva a mean height of 1.552 ± 0.068 for the mid-septum and 1.316 ± 0.054 for the side septa. The corresponding values for the group with normal gingiva are 1.213 ± 0.070 and 1.005 ± 0.050. The respective differences for the middle septum 0.339 ± 0.098 and for the side septa 0.311 ± 0.074, are statistically significant.

Taking into consideration the sex distribution (table 19), we find that the means for female smokers with healty gingiva are 1.3 mm for the middle septum and 1.0 mm for the side septa, while the corresponding values for males are 1.2 and 1.0 mm. Female smokers with gingiva changes show levels of 1.4 mm if they are light smokers and 1.6 mm if they are heavy smokers, which figures apply to the mid-septum 1.3, 1.5 and 1.9 mm, according to the degree of smoking, and for the side septa 1.1, 1.3 and 1.7 mm.

In considering the smokers' situation according to sex it must be remembered that the women are much fewer than the men in the total series. Women constituted not quite $^1/_3$ of the smokers with healthy gingiva and less than $^1/_5$ of those with changed gingiva. On the other hand, the range of variation is smaller for women than for men. No significant or probable sex differences exist. However, the tendency in both sexes to septal reduction parallelling the severity of smoking should be noted. Here there is a probable difference between non-smoking and heavily smoking men with diseased gingiva.

Table 19. Levels of the septa in smokers and non-smokers distributed according to sex. Collum projection.

Smoking	State of the gingiva											
	Normal						Diseased					
	Middle septum			Side septa			Middle septum			Side septa		
	Number	$M \pm \varepsilon (M)$	σ	Number	$M \pm \varepsilon (M)$	σ	Number	$M \pm \varepsilon (M)$	σ	Number	$M \pm \varepsilon (M)$	σ
					Men							
Non-smokers . . .	77	1.108 ± 0.083	0.380	119	0.916 ± 0.034	0.366	67	1.582 ± 0.106	0.864	111	1.250 ± 0.076	0.800
Light smokers . . .	31	1.194 ± 0.012	0.649	40	1.065 ± 0.084	0.530	43	1.321 ± 0.098	0.641	71	1.114 ± 0.068	0.573
Moderate smokers .	37	1.238 ± 0.095	0.580	58	0.945 ± 0.071	0.537	52	1.500 ± 0.099	0.712	79	1.276 ± 0.080	0.707
Heavy smokers. . .	9	1.178	—	13	1.092 ± 0.143	0.517	35	1.911 ± 0.153	0.904	47	1.687 ± 0.138	0.947
Total number of smokers . . .	77	1.213 ± 0.070	0.618	111	1.005 ± 0.050	0.532	130	1.552 ± 0.068	0.776	197	1.316 ± 0.054	0.759
					Women							
Non-smokers . . .	81	1.285 ± 0.053	0.477	125	1.002 ± 0.038	0.419	37	1.338 ± 0.092	0.563	59	1.164 ± 0.061	0.466
Light smokers . . .	18	1.344 ± 0.075	0.317	27	0.978 ± 0.074	0.386	16	1.369 ± 0.122	0.489	25	1.232 ± 0.071	0.384
Moderate smokers .	11	1.255 ± 0.222	0.735	17	1.112 ± 0.168	0.691	16	1.606 ± 0.154	0.615	26	1.304 ± 0.130	0.662
Heavy smokers. . .	2	1.800	—	4	1.150	—	1	1.600	—	2	1.100	—
Total number of smokers . . .	31	1.342 ± 0.096	0.535	48	1.040 ± 0.075	0.518	33	1.491 ± 0.096	0.551	53	1.262 ± 0.071	0.516

Interdental Septa in Persons with Normal Gingiva.

Having described the results we were able to obtain as regards certain minor problems, we shall now return to the main problem and discuss interdental septa in persons whose gingiva were considered healthy.

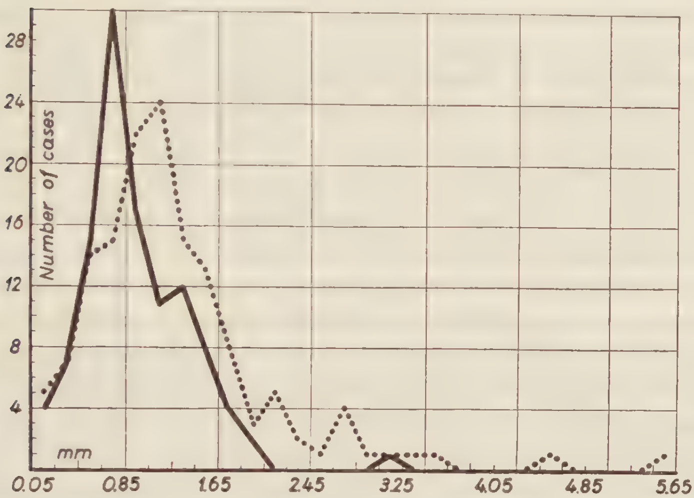


Fig. 1. The levels of the side septa (2– 1–) in men with normal gingiva (whole line) and in men with diseased gingiva (dotted line).

Fig. 1 shows the distribution of interdental septa in men with normal and diseased gingiva. It will be seen that a few persons' septa reach the enamel-cementum junction. Mostly the septa reach to a little bit more than 1 mm from this junction. Besides, the mean height of the middle septum is lower than the mean for the side septa. In a small number of persons the interdental septa were distinctly low with distances to the enamel-cementum junction of 2 to 3 mm, the middle septum still being lowest. This result may have three different causes.

1. The interdental septa in normals vary and never reach the enamel-cementum junction in most adults, but miss it by a considerable margin in some.

2. Originally reaching the enamel-cementum junction, the interdental septa have later been reduced, which may be regarded as normal atrophy in the examined age group.

3. In a large number of persons the interdental septa are subject to a reduction which must be considered pathologic.

It is difficult to say anything definite concerning the first possibility as no similar investigation has yet been performed. A final answer would require series of younger persons. A colleague, Dr. *Ekström*, is at present, however, busy on an investigation into certain problems concerning children and has roentgenographed their teeth. He has very kindly let me take measurements on 25 roentgenographs from children aged 7, a courtesy for which I thank him sincerely. The pictures were, however, differently projected, necessitating a reduction of the measurements in view of the established significant differences between apical and collum projection. Having performed these interpolations. one finds that the central septa on an average lie 0.47 mm below the enamel-cementum junction In some cases, however, the teeth were not fully erupted. and the enamel-cementum junction sometimes lay below the highest point on the interdental septum. After elimination of these cases. the series included 16 persons. The mean distance was now 0.52 mm. In one case it was 1.7 mm. The mean distance for the left side septum was 0.13 mm, with a maximum of 1.7 mm. The corresponding figures for the right side were 0.42 mm and 1.9 mm.

Although the small number of roentgenographs prevents this result from being accorded overdue importance, it was rather surprising. The fact that the distance between the enamel-cementum junction can be so large during infancy perhaps indicates that the found deviations in a series of adult normals are a sign that the situation agrees with the first of the three possibilities given above: that for many persons it is normal that septa despite fully erupted teeth never reach the enamel-cementum junction. It must be emphasized, however, that definite conclusions cannot be drawn until a large number of children have been examined.

We shall later return to the second possibility. and with respect to this and the event of pathologic reduction, we should like to state the following: the assumption would imply that the test persons at some earlier time had sustained a pathologic process—an inflammation—that had caused destruction of bone and then healed.

However, in persons as young as those in our series it is hardly credible that reduction for that reason should have been present to an extent sufficient to explain the result. For this would mean that very few people escape gingival inflammations resulting in destruction of bone before they are twenty years old. Experience tells us that such conditions hardly can be typical of youth in general, which does not, of course, preclude an instance or two of such processes.

The second possibility stands out as the most probable one: that already before age 20 the interdental septa to a certain extent are subject to normal atrophy. The rate of atrophy varies from person to person and therefore the interdental septa vary in height. However, I should like to stress that this problem cannot be cleared up conclusively without extensive studies with recourse to far larger series of test persons at age levels above and below the group available to us here.

Interdental Septa in Persons with Changed Gingiva.

In this group the distribution of the measurements shows the following: The bone reduction is greater than in the group with normal gingiva, although a small number of the individuals' interdental septa reached to the level of the healthy group. This is hardly surprising as cases of doubtful gingiva changes were included in the group. Moreover, some of the observed gingiva lesions may have been temporary and without effects on the bone. Some persons in this group, on the other hand, had very markedly reduced septa although the series included no severe cases of gingival disease, such as suppuration. The results afford no clue to the problem whether the morbid processes in the gingiva directly cause dissolution of bone or whether they merely speed up the rate of atrophy of the jawbone assumed to be normal in man.

In order to express in terms of numbers the significance of the gingiva changes, we have performed an appropriate computation (table 20).

Let us assume that the person in the group with gingival changes have normal septa whose septal distance from the enamel-cementum junction is less than the mean septal distance in the group with normal gingiva. Let us further calculate how many persons in the diseased group ought to exceed the mean if conditions were the same as in the healthy group. Table 20 gives the percentage of persons

Table 20. Theoretically calculated percentual number of individuals in the group with diseased gingiva whose septal levels exceed the mean. (Cf. the text.)

Septum	Total number with diseased gingiva	$P \pm \varepsilon$ (P)
	Men	
2–1–	144	36.2 ± 4.0
1–1	197	36.5 ± 3.4
–1–2	164	36.3 ± 3.8
	Women	
2–1–	52	35.0 ± 6.6
1–1	71	10.0 ± 3.6
–1–2	62	25.0 ± 5.5

remaining, which percentage may be regarded as an approximate measure of the effect of the gingival changes. The figure for men is approximately 35 per cent and for women it is slightly less. From this point of view we maintain that at about age 20 gingival changes affect the interdental septa to the extent mentioned, i. e. about 65 per cent of our test persons with gingival changes did not have abnormal interdental septa.

As long as the destruction of bone differs little from the extent in those we have permitted ourselves to regard as normal it is obviously difficult to say whether such destruction is pathologic or, rather, the result of normal atrophy that for some reason is accelerated. A high degree of reduction would in the latter case be the normal thing in old persons without gingival changes. This is another illustration of the necessity to study the high age groups. It should be noted, finally, that gingival changes are so universal as to be almost normal, just as smoking nowadays is considered almost "normal". An important result of this investigation—quite apart from any personal feelings concerning smoking—is that the tobacco habit is bad not only for the gingiva bot also for the interdental septa. The reservation that must be made is that the effect of tobacco may be more pronounced in young and inexperienced smokers than in "inveterates". In other words, the tissues may gradually become conditioned to tobacco, so that the latter no longer irritates the gingiva or affects the interdental septa.

* * *

The expenses of this study were met by a grant from the State funds for research at the Institute of Dentistry. Herefore I extend my respectful thanks to the University Chancellor and the Professorial Board. Professor *Gunnar Dahlberg* of the State Institute for Human Genetics and Race Biology at Uppsala has given me extremely valuable advice concerning the statistical analysis. He also made available facilities for the statistical computations. I am deeply grateful to Professor *Dahlberg* and I offer him my sincere thanks. I also wish to express my gratitude to my collaborators at the Roentgen Department of the Institute of Dentistry, Stockholm, for valuable assistance with some routine measurements, particularly in deciding the errors of method.

Summary.

The study embraces a series of 390 men and 216 women students at the Institute of Dentistry, Stockholm. Two different roentgen projections were used, one called the apical and one the collum method. The latter turned out to yield better results. The following were the chief results:

1. Gingival changes were more frequent in men than in women. They were far commoner in smokers than in non-smokers, and the found sex difference with respect to gingival changes may be due to the fact that men oftener smoke than do women.

2. Also between persons with and persons without dental deposits there was a significant difference in the frequency of gingival changes.

On the other hand, there was no significant difference between persons with anomalous teeth and persons with normally arranged teeth.

The investigation provided no definite information concerning the effect of environment during pre-school life and of exercise.

3. The central aim of the investigation was to gain knowledge concerning the variations of the interdental septa. In the roentgenographs the septal height was measured in relation to the enamel-cementum junction. It was found that the septal height in persons with *normal gingiva* varied considerably; in solitary instances this distance was as much as 3.5 mm. In persons with *diseased gingiva* the range of variation was still greater. Under certain conditions it may be said that about $^1/_3$ of the test persons with changed gingiva had reduced interdental septa.

4. A small series of 8-year-olds was also studied. It was found that not even in them did the interdental septa always reach to the enamel-cementum junction. The found variations in septal height in the series of adults may consequently be an expression of normal conditions and not caused by any secondary atrophy. The low interdental septa in persons with normal gums would less likely be due to pathologic processes. However, it is impossible to make definite statements before other age classes have been studied.

If means are computed for the test persons considered as having normal gingiva—about half the total series—the middle septum will be found to lie 1.22 ± 0.03 and the side septa respectively 0.96 ± 0.03 mm and 1.00 ± 0.03 mm below the approximal enamel margin.

5. In the test group with changed gingiva a significant difference in height was obtained for both the mid-septum and one of the side septa, when heavy and light smokers were compared. A significant difference was also obtained as regards the two side septa combined, when heavy smokers were compared with non-smokers. Finally, a probable difference was found to exist in non-smokers plus light smokers compared with moderate smokers plus heavy smokers.

6. It is surprising that about 13 per cent of the total number of examined persons had *dental deposits* without showing gingival changes, and that these persons also had considerably reduced septa compared to persons with normal gingiva and no deposits.

7. As regard the septal level no significant differences was found between persons with anomalous teeth and persons with normally arranged teeth, but there was a significant difference in the group with normal gingiva between persons with crowded teeth and persons with spaced teeth.

Résumé.

L'étude comprend une série de 319 étudiants et 216 étudiantes de l'Institut dentaire de Stockholm.

Deux méthodes différentes de projection radiographique ont été appliquées, l'une fut appelée méthode apicale et l'autre méthode de collet. Cette dernière s'est révélée donner de meilleurs résultats. Les conclusions furent les suivantes:

1. Les altérations gingivales sont plus fréquentes chez les hommes que chez les femmes, et leur nombre est plus élevé chez les fumeurs que chez les non-fumeurs. Il est possible que cette différence soit due au fait que les hommes sont plus souvent des fumeurs que les femmes.

2. Il existe aussi une différence significative dans la fréquence des altérations gingivales entre des personnes avec ou sans dépôts dentaires. D'autre part, il n'y a pas de différence significative entre des personnes ayant une disposition anormale et normale des dents.

Les investigations ne donnent pas d'information définitive concernant l'effet du milieu extérieur pendant la vie préscolaire et de l'exercice physique.

3. Le but principal des recherches consiste à acquérir des connaissances concernant les variations des parois alvéolaires. On mesure par des radiographies la hauteur de ces parois par rapport à la limite cemento-adamantine. Il se révèle que la hauteur de cette paroi varie considérablement chez des personnes avec des gencives normales; dans quelques cas, la distance est même de 3,5 mm. Chez des personnes avec des gencives altérées, le degré de variation peut être encore plus grand. Sous certaines conditions on peut dire qu'environ un tiers des personnes examinées avec des gencives altérées ont des parois alvéolaires hypotrophiques.

4. Un petit groupe d'enfants de huit ans ont également été examinés. On constate que même chez eux la hauteur des parois alvéolaires n'arrive pas toujours à la limite cemento-adamantine. Les variations de hauteur de cette paroi trouvées chez les adultes doivent par conséquent être l'expression de conditions normales et non causées par une atrophie secondaire.

Les parois alvéolaires basses chez des personnes avec des gencives normales sont encore moins dues à des processus pathologiques. Cependant, il est impossible de tirer des conclusions définitives avant que d'autres classes d'âges soient examinées. Si l'on calcule la valeur moyenne des personnes examinées, dont les gencives sont considérées être normales (à peu près la moitié de la série totale), on trouve que le septum médian est situé à $1{,}22 \pm 0{,}03$ mm et la paroi latérale $0{,}96 \pm 0{,}03$ mm et $1{,}00 \pm 0{,}03$ mm respectivement sous le bord approximatif de l'émail.

5. Dans le groupe examiné avec altération des gencives, une différence significative de la hauteur a été obtenue aussi bien pour le

septum médian que pour une des parois latérales si on compare les gros fumeurs aux petits fumeurs. Une différence significative a également été obtenue en ce qui concerne la combinaison des deux parois latérales, si on compare de gros fumeurs aux non-fumeurs. Enfin, une différence semble exister entre le total de non-fumeurs plus petits fumeurs, comparés au total de fumeurs modérés plus gros fumeurs.

6. Il est surprenant qu'environ 13% du nombre total des personnes ont des dépôts dentaires sans montrer des altérations gingivales et que ces personnes ont également des parois alvéolaires hypotrophiques en comparaison aux personnes dont les gencives sont normales et sans tartre dentaire.

7. En ce qui concerne la hauteur de la paroi alvéolaire, on n'a pas pu mettre en évidence des différences significatives entre des personnes avec des dents anormalement et normalement disposées. Cependant il existe une différence significative dans le groupe avec des gencives normales entre des individus ayant des dents serrées et des individus aux dents espacées.

Zusammenfassung.

Die vorliegende Untersuchung wurde an 319 Studenten und 216 Studentinnen der zahnärztlichen Hochschule in Stockholm ausgeführt. Hierbei wurden zwei verschiedene Projektionsmethoden angewandt, von denen die eine die apicale, die andere die Collummethode genannt wurde. Letzere ergab, wie sich herausstellte, bessere Resultate. Die wichtigsten Resultate sind folgende:

1. Veränderungen des Zahnfleisches kamen häufiger bei Männern als bei Frauen vor. Zahnfleischveränderungen traten häufiger bei Rauchern als bei Nichtrauchern auf, und es ist möglich, daß der Unterschied zwischen den Geschlechtern im Hinblick auf Zahnfleischveränderungen darauf beruht, daß Männer häufiger als Frauen Raucher sind.

2. Es wurde außerdem ein statistisch sichergestellter Unterschied im Vorkommen von Zahnfleischveränderungen beim Vergleich von Personen mit und ohne Zahnstein gefunden.

Dagegen konnte kein sicherer Unterschied zwischen Personen mit Zahnstellungsanomalien und solchen mit normaler Zahnstellung gefunden werden.

Die Untersuchung gibt keine Aufklärung über die Bedeutung des Milieus im vorschulpflichtigen Alter noch über die Bedeutung von Leibesübungen.

3. Die Hauptaufgabe der Untersuchung war, Einblick in das Verhalten des Zahnseptums zu bekommen. Die Höhe des Septums im Verhältnis zur Email-Zementgrenze wurden auf Röntgenbildern gemessen. Es zeigte sich, daß die Höhe der Zahnsepta bei Personen mit *normalem Zahnfleisch* erheblich variiert. In einzelnen Fällen war der Abstand sogar 3,5 mm. Bei Personen mit Zahnfleischveränderungen erhielt man eine noch größere Variation und Extremwerte. Von gewissen Voraussetzungen ausgehend, kann man sagen, daß ungefähr ein Drittel aller Versuchspersonen mit Zahnfleischveränderungen reduzierte Zahnpasta haben.

4. Es wurde auch eine kleinere Anzahl Siebenjähriger untersucht. Nicht einmal bei diesen fand man, daß die Zahnsepta immer bis zur Email-Zementgrenze reichte. Es ist daher möglich, daß die gefundene Variation in bezug auf die Höhe der Zahnsepta in der Serie der Erwachsenen ein Ausdruck für normale Verhältnisse ist und nicht der einer sekundären Atrophie. Noch weniger wahrscheinlich ist, daß die niedrigen Zahnsepta bei Personen mit normalem Zahnfleisch von pathologischen Prozessen verursacht werden. Man kann allerdings nichts mit Bestimmtheit sagen, bevor nicht Untersuchungen an anderen Altersgruppen durchgeführt worden sind.

Berechnet man den Mittelwert für die untersuchten Personen, deren Zahnfleisch als normal angesehen wurde und die ungefähr die Hälfte des Untersuchungsmateriales ausmachen, so findet man, daß das *Mitt-Septum* $1{,}22 \pm 0{,}03$ mm und die Seitensepta $0{,}96 \pm 0{,}03$ mm resp. $1{,}00 \pm 0{,}03$ mm unter der approximalen Emailkante liegen.

5. In der Versuchsgruppe mit Zahnfleischveränderungen erhielt man statistisch sichere Unterschiede in der Höhe teils beim *Mitt-Septum* und teils bei einem der Seitensepta beim Vergleich starke und schwache Raucher. Bei dem Vergleich starke Raucher und Nichtraucher ergab sich ein statistisch sicherer Unterschied im Hinblick auf beide Seitensepta zusammen. Schließlich wurde auch ein statistisch wahrscheinlicher Unterschied zwischen Nichtrauchern plus schwachen Rauchern und mäßigen plus starken Rauchern gefunden.

6. Es ist überraschend, daß ungefähr 13 % sämtlicher untersuchter Personen *Zahnsteinbelag* aufwiesen ohne daß das Zahnfleisch verändert war. Diese Personen hatten auch wesentlich verminderte Septa verglichen mit jenen mit normalem Zahnfleisch und ohne Zahnstein.

7. Es konnte kein sicherer Unterschied in bezug auf die Höhen der Septa beim Vergleich zwischen Personen mit normaler Zahnstellung und solchen mit Zahnstellungsanomalien gefunden werden. Innerhalb der Gruppe mit normalem Zahnfleisch zeigte sich dagegen ein statistisch sicherer Unterschied beim Vergleich zwischen Personen mit dichtstehenden und solchen mit auseinanderstehenden Zähnen.